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(54) Title: OXAZOLIDINONE COMBINATORIAL LIBRARIES, COMPOSITIONS AND METHODS OF PREPARATION			
(57) Abstract  Oxazolidinones and methods for their synthesis are provided. Also provided are combinatorial libraries comprising oxazolidinones, and methods to prepare the libraries. Further provided are methods of making biologically active oxazolidinones as well as pharmaceutically acceptable compositions comprising the oxazolidinones. The methods of library preparation include the attachment of oxazolidinones to a solid support. The methods of compound preparation in one embodiment involve the reaction of an iminophosphorane with a carbonyl containing polymeric support.			

## CLAIMS

What is claimed is:

1. A method for the solid phase synthesis of oxazolidinones, comprising the steps of:

- a) attaching an olefin to a solid support;
- b) oxidizing the olefin to provide an epoxide functionality;
- c) opening the epoxide with an amine to form an amino alcohol; and
- d) cyclizing the amino alcohol using a phosgene equivalent.

2. The method according to claim 1, where the olefin is an allylic amine or allylamine.

3. The method according to claim 1, where the amine is an amino acid, or an aromatic amine.

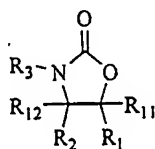
4. A method for the synthesis of oxazolidinone combinatorial libraries, comprising the steps of:

- a) attaching an olefin group to an array of solid supports;
- b) oxidizing the individual olefin groups to provide an array of solid support bound epoxides; and
- c) opening the epoxide with an amine to form an amino alcohol; and
- d) cyclizing the amino alcohol using a phosgene equivalent.

5. The method according to claim 4, where the olefin is an allylic amine, or allylamine.

6. The method according to claim 4, where the amine units are amino acids or aromatic amines.

7. An oxazolidinone combinatorial library, where the oxazolidinones comprising the library are of the following structure:



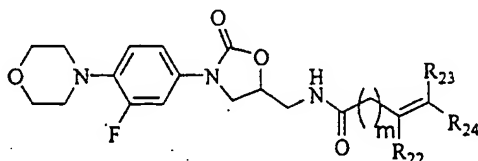
1a

where  $R_1$  is selected from the group consisting of alkyl, heteroalkyl, aryl and heteroaryl,  $R_2$  is selected from the group consisting of hydrogen, alkyl, heteroalkyl, aryl and heteroaryl,  $R_3$  is selected from the group consisting of hydrogen, alkyl, heteroalkyl, aryl and heteroaryl,  $R_{11}$  is selected from the group consisting of hydrogen, alkyl, heteroalkyl, aryl and heteroaryl, and  $R_{12}$  is selected from the group consisting of hydrogen, alkyl, heteroalkyl, aryl and heteroaryl.

8. The combinatorial library according to claim 7, where  $R_3$  is selected from the group consisting of aryl and heteroaryl, and further where the aryl and heteroaryl groups are the aryl and heteroaryl groups attached to the amines of Table 2 and Figures 29, 30, and 31.

9. The combinatorial library according to claim 7, where  $R_3$  is a heteroaryl group selected from the group consisting of a pyridyl group, a thienylphenyl group, an oxazolyl group, a pyrrolyl group, and a morpholinofluorophenyl group.

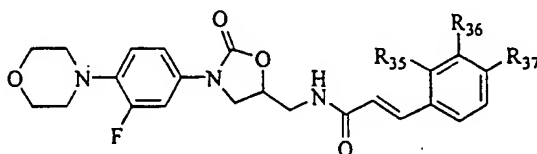
10. An antimicrobial compound where the compound is of the structure:



where  $m$  is 0, 1, 2 or 3, and where  $R_{22}$ ,  $R_{23}$  and  $R_{24}$  are independently selected from the group consisting of hydrogen, alkyl, heteroalkyl, aryl and heteroaryl.

11. The antimicrobial compound according to claim 10, where  $m$  is 0, and where  $R_{22}$  and  $R_{23}$  are hydrogen, and where  $R_{24}$  is an aryl group.

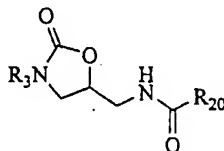
12. The antimicrobial compound according to claim 11, where the compound is of the structure:



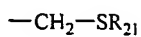
where  $R_{35}$ ,  $R_{36}$  and  $R_{37}$  are independently selected from the group consisting of hydrogen, electron withdrawing group, alkyl, heteroalkyl, aryl and heteroaryl.

13. An antimicrobial compound, where the compound has the following structure:

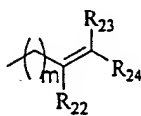
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where  $R_3$  is selected from the group consisting of aryl and heteroaryl, and where  $R_{20}$  is selected from the group consisting of structures A, B, C, I, J and K

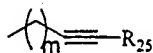


A

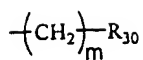


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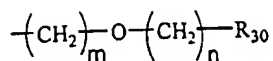
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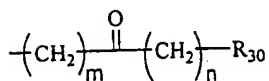
C



I



J



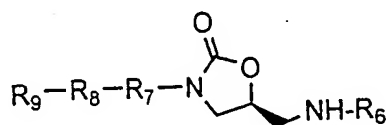
K

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wherein m is 0, 1, 2 or 3, and where n is 0, 1, 2 or 3, and wherein R<sub>21</sub> is selected from the group consisting of alkyl, heteroalkyl, aryl and heteroaryl, and where R<sub>22</sub>, R<sub>23</sub> and R<sub>24</sub> are independently selected from the group consisting of hydrogen, alkyl, heteroalkyl, aryl and heteroaryl, and where R<sub>25</sub> is selected from the group consisting of hydrogen, alkyl, heteroalkyl, aryl and heteroaryl, and where R<sub>30</sub> is selected from the group consisting of alkyl, heteroalkyl, aryl and heteroaryl.

10

14. A compound of formula 2c:



15

2c

wherein:

R<sub>6</sub> is acyl or sulfonyl;

R<sub>7</sub> is aryl or heteroaryl;

$R_8$  is  $C_1$ - $C_7$  alkyl, NR, O, S,  $C(=O)NR$ ,  $NRC(=O)$ ,  $C(=O)$ ,  $C(=O)O$ ,  $OC(=O)$ ,  $S(=O)$ ,  $SO_2$ ,  $SO_2NR$ ,  $NRSO_2$ ,  $NRCONR'$ , or  $(CH_2)_nO$ , wherein  $n = 0-6$ , and wherein R and R' are independently H, alkyl, heteroalkyl, aryl or heteroaryl; and

$R_9$  is hydrogen, OH, alkyl, aryl, heteroalkyl, or heteroaryl.

15. The compound of claim 14 wherein:

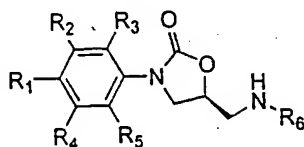
$R_6$  is  $C(=O)R$ , wherein R is H, alkyl, or aryl;

$R_7$  is aryl;

$R_8$  is  $NH(C=O)$  or  $NR'(C=O)$ , where R' is H, alkyl, or aryl; and

$R_9$  is hydrogen, pyridinyl, thiazolyl, benzothiazolyl, isothiazolyl, quinolinyl, 1,3,4-triazolyl, or 1,3,4-thiadiazolyl.

16. A compound of the structure 1b:



1b

wherein  $R_2$ ,  $R_3$ ,  $R_4$  and  $R_5$  are, independently, hydrogen, alkyl, heteroalkyl, heteroaryl or an electron withdrawing group;  $R_6$  is acyl or sulfonyl; and,  $R_1$  is one of the following functional groups:  $C(O)NR_7R_8$ , wherein  $R_7$  and  $R_8$  are, independently, hydrogen, alkyl, heteroalkyl, aryl or heteroaryl;  $C(O)OR_9$ , wherein  $R_9$  is hydrogen, alkyl, heteroalkyl, aryl or heteroaryl;  $C(O)R_{10}$ , wherein  $R_{10}$  is hydrogen, alkyl, heteroalkyl, aryl or heteroaryl;  $SR_{11}$ , wherein  $R_{11}$  is hydrogen, alkyl, heteroalkyl, aryl or heteroaryl;  $S(O)_2R_{11}$ , wherein  $R_{11}$  is hydrogen, alkyl, heteroalkyl, aryl or heteroaryl;  $S(O)R_{11}$ , wherein  $R_{11}$  is hydrogen, alkyl, heteroalkyl, aryl or heteroaryl;  $NR_{12}R_{13}$ , wherein  $R_{12}$  and  $R_{13}$  are, independently, hydrogen, acyl, sulfonyl, alkyl, heteroalkyl, aryl or heteroaryl; 2-oxazolyl, wherein  $R_{14}$  is at the 4-position and  $R_{15}$  is at the 5-position of the oxazolyl, and wherein  $R_{14}$

and  $R_{15}$  are, independently, hydrogen, alkyl, heteroalkyl, aryl, heteroaryl or an electron withdrawing group; 2-aminothiazolyl, wherein  $R_{16}$  is at the 4-position and  $R_{17}$  is at the 5-position of the thiazole, and wherein  $R_{16}$  and  $R_{17}$  are, independently, hydrogen, alkyl, heteroalkyl, aryl, heteroaryl or an electron withdrawing group; and,  $\text{CH}_2\text{NR}_{18}\text{R}_{19}$ , wherein  $R_{18}$  and  $R_{19}$  are, independently, hydrogen, alkyl, heteroalkyl, aryl, heteroaryl, acyl or sulfonyl.

17. A combinatorial library of compounds according to claim 16.
18. A compound of claim 16, wherein  $R_1$  is  $\text{C(O)NR}_7\text{R}_8$ ,  $\text{C(O)OR}_9$ ,  $\text{C(O)R}_{10}$ ,  $\text{SR}_{11}$ ,  $\text{S(O)}_2\text{R}_{11}$ ,  $\text{S(O)R}_{11}$  or  $\text{NR}_{12}\text{R}_{13}$ .
19. A compound according to claim 16, wherein  $R_1$  is  $\text{C(O)NR}_7\text{R}_8$ .
20. A compound according to claim 16, wherein  $R_1$  is  $\text{C(O)OR}_9$ .
21. A compound according to claim 16, wherein  $R_1$  is  $\text{C(O)R}_{10}$ .
22. A compound according to claim 16, wherein  $R_1$  is  $\text{SR}_{11}$ .
23. A compound according to claim 16, wherein  $R_1$  is  $\text{NR}_x(\text{C=O})\text{R}_y$ , wherein  $R_x$  and  $R_y$  are independently hydrogen, alkyl, heteroalkyl, aryl, or heteroaryl.
24. A compound according to claim 16, wherein  $R_1$  is  $\text{NR}_x(\text{SO}_2)\text{R}_y$ , wherein  $R_x$  and  $R_y$  are independently hydrogen, alkyl, heteroalkyl, aryl, or heteroaryl with the proviso that  $R_y$  is not H.
25. A compound according to claim 16, wherein  $R_1$  is  $\text{NR}_{12}\text{R}_{13}$ .
26. A compound according to claim 16, wherein  $R_1$  is 2-oxazolyl, wherein  $R_{14}$  is at the 4-position and  $R_{15}$  is at the 5-position of the oxazole group.
27. A compound according to claim 16, wherein  $R_1$  is 2-aminothiazolyl, wherein  $R_{16}$  is at the 4-position and  $R_{17}$  is at the 5-position of the aminothiazolyl group.
28. A compound according to claim 16, wherein  $R_1$  is  $\text{CH}_2\text{NR}_{18}\text{R}_{19}$ .
29. A compound according to claim 18; wherein  $R_3$ ,  $R_4$  and  $R_5$  are hydrogen.
30. A compound according to claim 29, wherein  $R_2$  is fluorine.
31. A compound according to claim 30, wherein  $R_6$  is  $\text{C(O)CH}_3$ .
32. A compound according to claim 31, wherein  $R_1$  is  $\text{C(O)NR}_7\text{R}_8$  and  $R_7$  is hydrogen.
33. A compound according to claim 32, wherein  $R_8$  is heteroaryl.
34. A biologically active oxazolidinone derived from a combinatorial library



according to claim 17.

35. A compound according to claim 19, wherein  $R_3$ ,  $R_4$  and  $R_5$  are hydrogen.
36. A compound according to claim 26, wherein  $R_3$ ,  $R_4$  and  $R_5$  are hydrogen.
37. A compound according to claim 27, wherein  $R_3$ ,  $R_4$  and  $R_5$  are hydrogen.
- 5 38. A compound according to claim 35, wherein  $R_2$  is fluorine.
39. A compound according to claim 36, wherein  $R_2$  is fluorine.
40. A compound according to claim 37, wherein  $R_2$  is fluorine.
41. A compound according to claim 38, wherein  $R_6$  is  $C(O)CH_3$ , and  $NR_7R_8$  is  $NH(5'-(5\text{-aminopyridine-2-yl})thiopyridine-3'\text{-yl})$  or  $NH(\text{pyridine-3-yl})$ .
- 10 42. A compound according to claim 38, wherein  $R_6$  is  $C(O)CH_2SMe$ , and  $NR_7R_8$  is  $NH(5\text{-chloropyridine-3-yl})$ .
43. A compound according to claim 38, wherein  $R_6$  is  $C(O)CHCH(\text{pyridine-3-yl})$ , and  $R_7R_8$  is  $NH(5\text{-chloropyridine-3-yl})$ .
44. A method of preparing the combinatorial libraries according to claim 17,
- 15 comprising the steps of:
- a) attaching a plurality of aryl oxazolidinones to a plurality of solid supports;
  - b) functionalizing the 4-position of the aryl groups of the attached oxazolidinones; and, optionally,
  - 20 c) removing the oxazolidinones from the solid supports.
45. The method according to claim 44, wherein the aryl oxazolidinone is attached to a solid support through the reaction of an iminophosphorane with a carbonyl containing resin to form an imine.
- 25 46. The method according to claim 44, wherein the aryl oxazolidinone is attached to a solid support through the reaction of an amine with a carbonyl containing resin to form an imine.
47. The method according to claim 45, wherein the attachment further comprises the step of reducing the imine.
48. The method according to claim 46, wherein the attachment further
- 30 comprises the step of reducing the imine.
49. A method of synthesizing the compounds according to claim 16, wherein

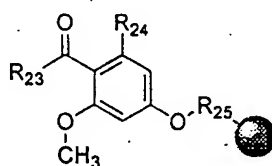
the method comprises the steps of:

- a) providing an iminophosphorane;
- b) mixing the iminophosphorane with a resin that comprises carbonyl groups to form an imine intermediate; and,
- c) reducing the imine intermediate to afford a compound attached to the resin through an amine linkage.

50. A method according to claim 49, wherein the iminophosphorane is provided from an azide that is reacted with a phosphine.

51. A method according to claim 49, wherein the iminophosphorane is provided from an amine that is reacted with a (trisubstituted)phosphine dihalide.

52. A method according to claim 49, wherein the resin comprising carbonyl groups is of the structure



1c

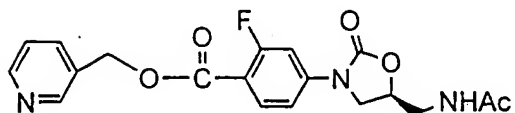
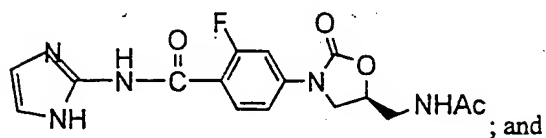
wherein  $R_{23}$  is hydrogen, alkyl, aryl, O-alkyl or O-aryl;  $R_{24}$  is hydrogen,  $\text{CH}_3\text{O}$  or  $\text{NO}_2$ ;  $R_{25}$  is  $(\text{CH}_2)_n\text{CONH}$ , wherein  $n$  is an integer between 1 and about 5; and, the filled circle is a polymeric support.

53. A method according to claim 52, wherein  $R_{23}$  is hydrogen,  $R_{24}$  is  $\text{CH}_3\text{O}$ ,  $R_{25}$  is  $(\text{CH}_2)_3\text{CONH}$ , and the filled circle is Tentagel, (cross-linked)polystyrene, (cross-linked)polyethyleneglycol or polyethyleneglycol-polystyrene compositions.

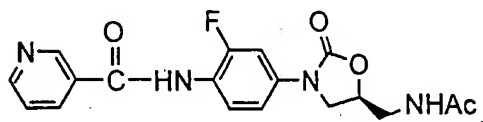
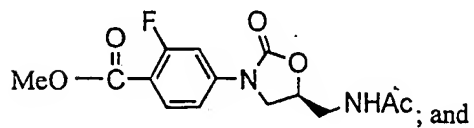
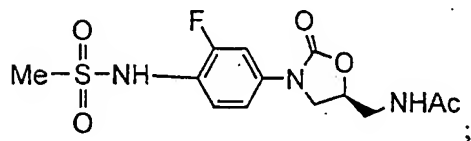
54. A method of synthesizing a compound according to claim 16, wherein the method comprises the steps of:

- a) reacting an amine with a resin that comprises carbonyl groups to form an imine intermediate; and
- b) reducing the imine intermediate to afford a compound attached to the resin through an amine linkage.

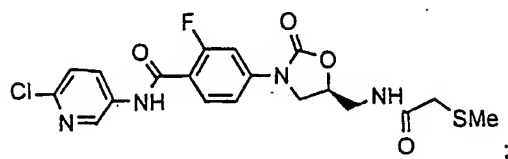
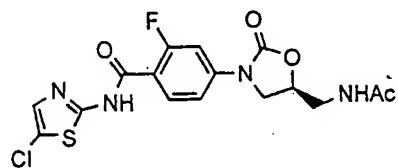
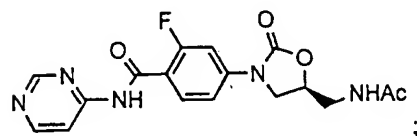
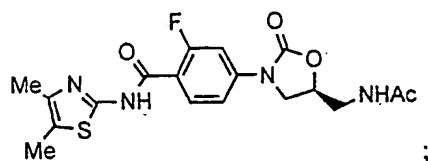
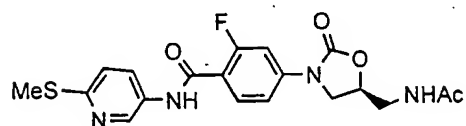
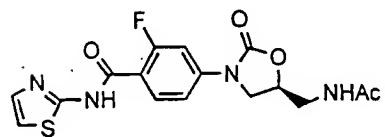
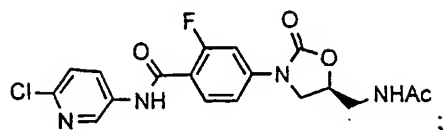
55. The compound of claim 14 selected from the group consisting of

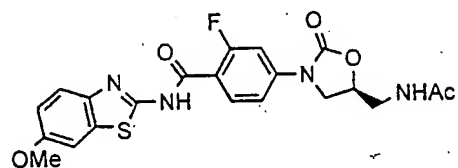
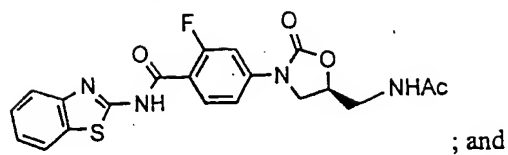


56. The compound of claim 14 selected from the group consisting of



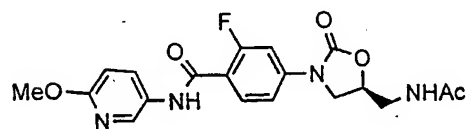
57. The compound of claim 14 selected from the group consisting of



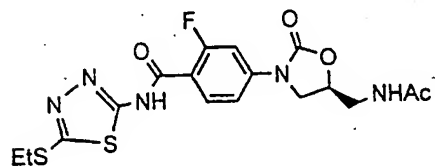
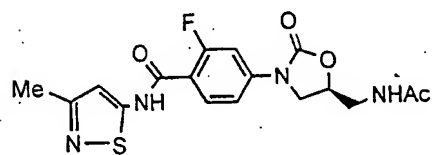
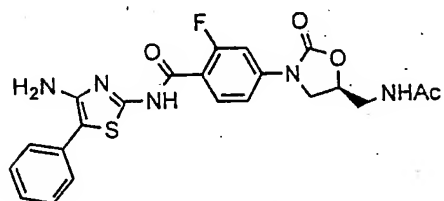


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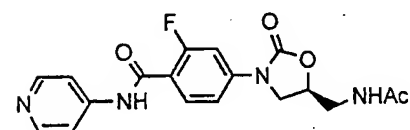
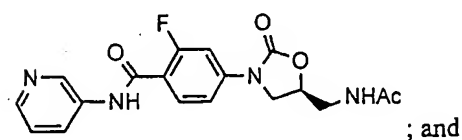
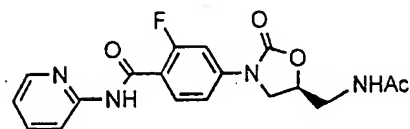
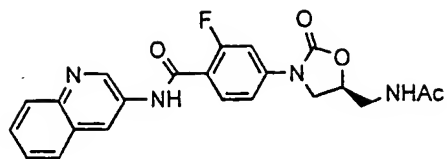
58. The compound of claim 14 selected from the group consisting of



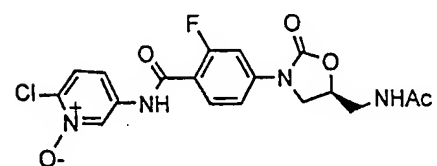
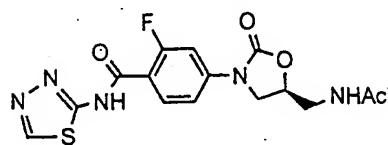
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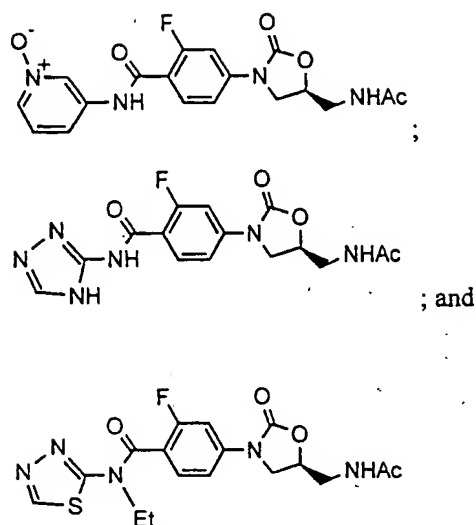


15



59. The compound of claim 14 selected from the group consisting of





5

60. The compound of claim 14 wherein:

$R_6$  is  $C(=O)R$ , wherein  $R$  is  $H$ , alkyl, heteroalkyl, aryl or heteroaryl;

$R_7$  is aryl;

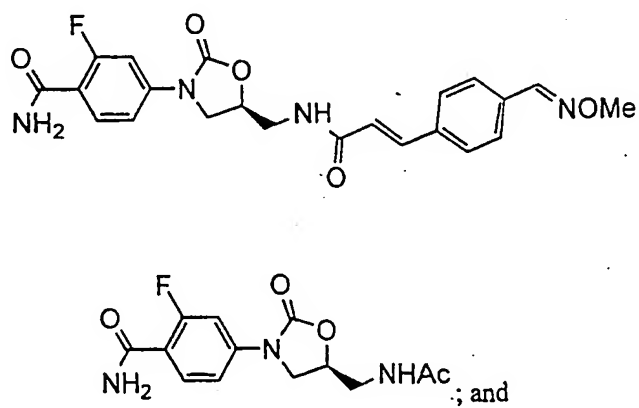
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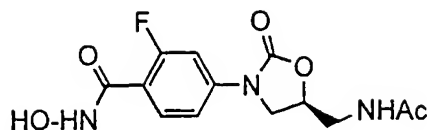
$R_8$  is  $NH(C=O)$ ; and

$R_9$  is hydrogen or  $OH$ .

61. The compound of claim 14 wherein the compound is selected from the group consisting of:

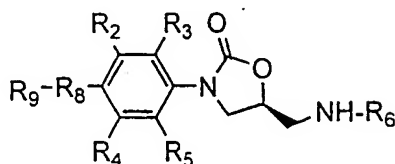
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62. A compound of formula 3c



3c

10

wherein:

$R_2$ ,  $R_3$ ,  $R_4$  and  $R_5$  are, independently, hydrogen, alkyl, heteroalkyl, heteroaryl or an electron withdrawing group;

$R_6$  is acyl or sulfonyl;

15

$R_8$  is  $C_1$ - $C_7$  alkyl, NR, O, S,  $C(=O)NR$ ,  $NRC(=O)$ ,  $C(=O)$ ,  $C(=O)O$ ,  $OC(=O)$ ,  $S(=O)$ ,  $SO_2$ ,  $SO_2NR$ ,  $NRSO_2$ ,  $NRCONR'$ , or  $(CH_2)_nO$ , wherein  $n = 0-6$ , and wherein R and R' are independently H, alkyl, heteroalkyl, aryl or heteroaryl; and

$R_9$  is alkyl, aryl, heteroalkyl, or heteroaryl.

20

63. The compound of claim 62, wherein

$R_6$  is  $C(=O)CH_3$ ;

$R_7$  is aryl;

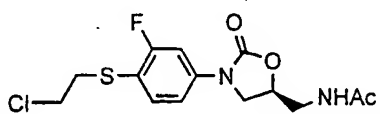
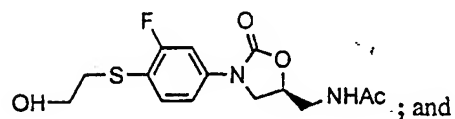
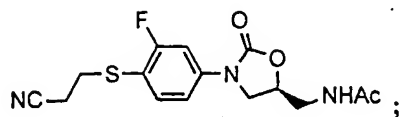
$R_8$  is S; and

$R_9$  is heteroalkyl.

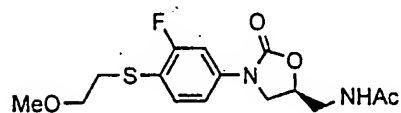
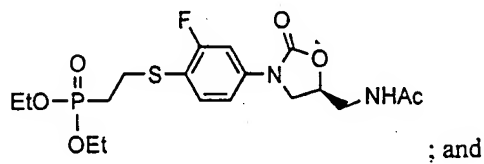
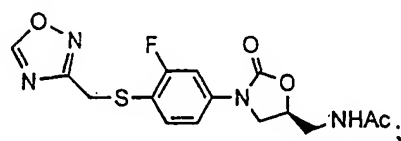
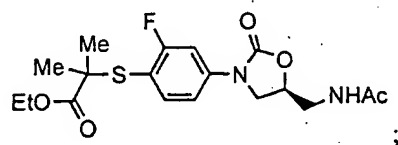
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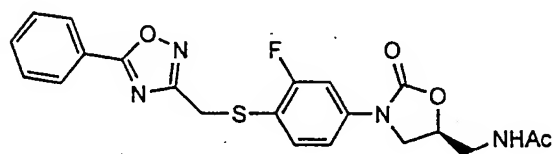
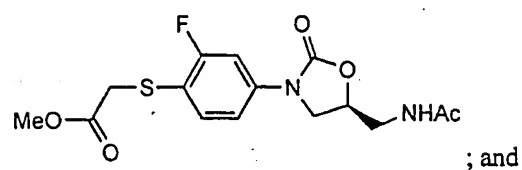
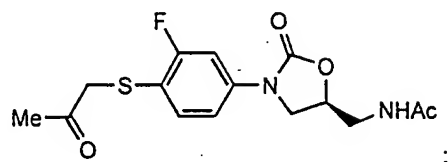
64. The compound of claim 62, wherein the compound is selected from the group consisting of



10 65. The compound of claim 62, wherein the compound is selected from the group consisting of



66. The compound of claim 62, wherein the compound is selected from the group consisting of



67. The compound of claim 62 wherein:

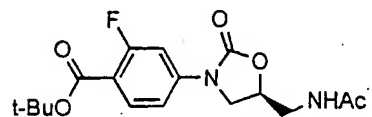
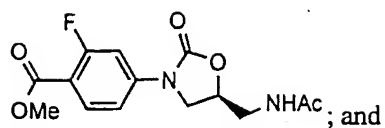
$R_6$  is  $C(=O)CH_3$ ;

$R_7$  is aryl;

$R_8$  is  $OC(=O)$ ; and

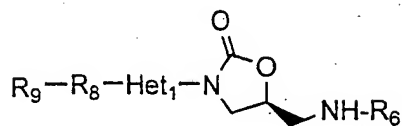
$R_9$  is alkyl.

68. The compound of claim 62 selected from the group consisting of:



5

69. A compound of formula 4c:



10

4c

wherein:

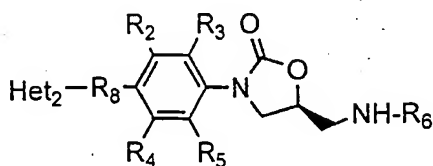
$R_6$  is acyl or sulfonyl;

$Het_1$  is heteroaryl;

$R_8$  is  $C_1$ - $C_7$  alkyl, NR, O, S,  $C(=O)NR$ ,  $C(=O)NOR$ ,  $NRC(=O)$ ,  $C(=O)$ ,  $C(=O)O$ ,  
 15  $OC(=O)$ ,  $S(=O)$ ,  $SO_2$ ,  $SO_2NR$ ,  $NRSO_2$ ,  $NRCONR'$ , or  $(CH_2)_nO$ , wherein  $n = 0-6$ , and  
 wherein R and R' are independently H, alkyl, heteroalkyl, aryl or heteroaryl; and  
 $R_9$  is alkyl, aryl, heteroalkyl, or heteroaryl.

70. A compound of formula 5c:

20



5c

wherein:

$R_2$ ,  $R_3$ ,  $R_4$  and  $R_5$  are, independently, hydrogen, alkyl, heteroalkyl, heteroaryl or an  
5 electron withdrawing group;

$R_6$  is acyl or sulfonyl;

$R_8$  is  $C_1$ - $C_7$  alkyl, NR, O, S,  $C(=O)NR$ ,  $NRC(=O)$ ,  $C(=O)NOR$ ,  $C(=O)O$ ,  
OC(=O),  $S(=O)$ ,  $SO_2$ ,  $SO_2NR$ ,  $NRSO_2$ ,  $NRCONR'$ , or  $(CH_2)_nO$ , wherein  $n = 0-6$ , and  
wherein R and R' are independently H, alkyl, heteroalkyl, aryl or heteroaryl; and

10  $Het_2$  is a heterocyclic group.

71. The compound of claim 70, wherein

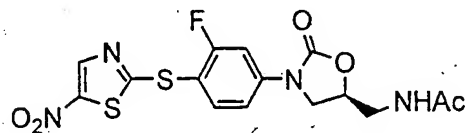
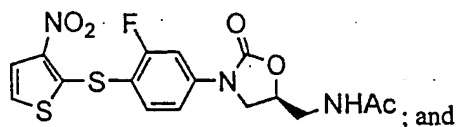
$R_6$  is  $C(=O)CH_3$ ;

$R_7$  is aryl;

15  $R_8$  is S; and

$Het_2$  is a thienylphenyl or thiazolyl group.

72. The compound of claim 70 selected from the group consisting of:



73. The compound of claim 70 wherein:

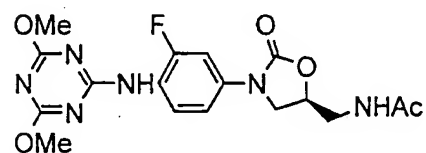
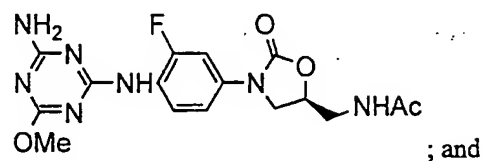
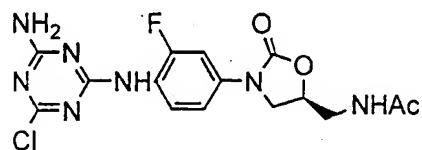
R<sub>6</sub> is C(=O)CH<sub>3</sub>;

R<sub>7</sub> is aryl;

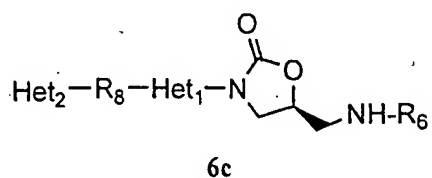
R<sub>8</sub> is NH; and

Het<sub>2</sub> is 1,3,5-triazinyl.

74. The compound of claim 70 selected from the group consisting of



75. A compound of formula 6c:



wherein:

$R_6$  is acyl or sulfonyl;

$R_8$  is  $C_1$ - $C_7$  alkyl, NR, O, S,  $C(=O)NR$ ,  $NRC(=O)$ ,  $C(=O)NOR$ ,  $C(=O)$ ,  $C(=O)O$ ,  $OC(=O)$ ,  $S(=O)$ ,  $SO_2$ ,  $SO_2NR$ ,  $NRSO_2$ ,  $NRCONR'$ , or  $(CH_2)_nO$ ,

wherein  $n = 0-6$ , and wherein R and R' are independently H, alkyl, heteroalkyl, aryl or heteroaryl;

Het<sub>1</sub> is heteroaryl; and

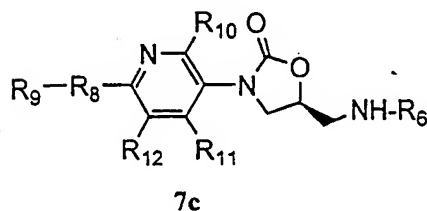
Het<sub>2</sub> is a heterocyclic group.

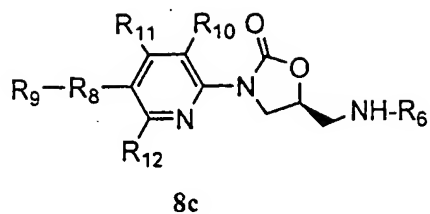
76. The compound of claim 75 wherein

Het<sub>1</sub> is selected from the group consisting of thienylphenyl, thiazolyl, 1,3,4-thiadiazolyl, pyridinyl, pyrimidinyl, phenyl and fluorophenyl; and

Het<sub>2</sub> is selected from the group consisting of oxazolyl, isoxazolyl, 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,3-oxadiazolyl, thienylphenyl, thiazolyl, isothiazolyl, 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,3,4-thiadiazolyl, pyrrolyl, imidazolyl, pyrazolyl, 1,2,3-triazolyl, 1,2,4-triazolyl, 1,2,3-triazinyl, 1,2,4-triazinyl, tetrazolyl, pyridinyl, pyrazinyl, pyrimidinyl, pyridazinyl, 1,2,4-triazinyl, 1,3,5-triazinyl, and 1,2,4,5-tetrazinyl.

77. A compound of formulas 7c or 8c:





wherein:

5

$R_6$  is acyl or sulfonyl;

$R_8$  is  $C_1$ - $C_7$  alkyl, NR, O, S,  $C(=O)NR$ ,  $C(=O)NOR$ ,  $NRC(=O)$ ,  $C(=O)$ ,  $C(=O)O$ ,  $OC(=O)$ ,  $S(=O)$ ,  $SO_2$ ,  $SO_2NR$ ,  $NRSO_2$ ,  $NRCONR'$ , or  $(CH_2)_nO$ , wherein  $n = 0-6$ , and wherein R and R' are independently H, alkyl, heteroalkyl, aryl or heteroaryl;

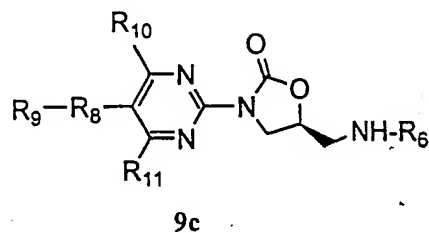
$R_9$  is alkyl, aryl, heteroalkyl, or heteroaryl; and

10

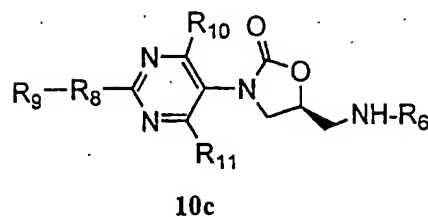
$R_{10}$ ,  $R_{11}$  and  $R_{12}$  are independently hydrogen, alkyl, aryl, heteroalkyl, electron withdrawing group, F, Cl, CN,  $NO_2$ ,  $NR''R'''$ ,  $OR''$ ,  $SR''$ ,  $S(=O)R''$ ,  $SO_2R''$ ,  $C(=O)R''$ ,  $C(=O)OR''$ ,  $OC(=O)R''$ ,  $C(=O)NR''R'''$ ,  $N(R'')C(=O)R'''$ , or N-oxide group in the pyridine nuclei, wherein  $R''$  and  $R'''$  are independently H, alkyl, heteroalkyl, aryl or heteroaryl.

15

78. A compound of formula 9c or 10c:



20



wherein:

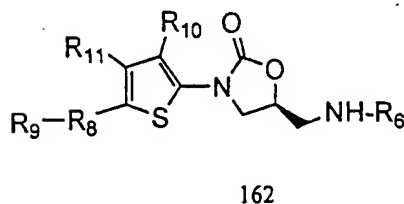
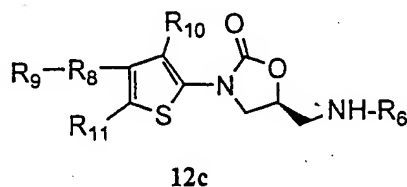
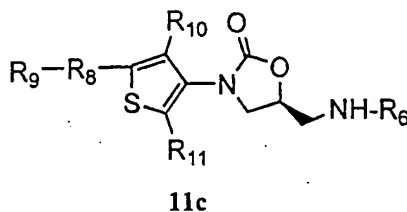
$R_6$  is acyl or sulfonyl;

$R_8$  is  $C_1$ - $C_7$  alkyl, NR, O, S,  $C(=O)NR$ ,  $C(=O)NOR$ ,  $NRC(=O)$ ,  $C(=O)$ ,  $C(=O)O$ ,  
 5  $OC(=O)$ ,  $S(=O)$ ,  $SO_2$ ,  $SO_2NR$ ,  $NRSO_2$ ,  $NRCONR'$ , or  $(CH_2)_nO$ , where  $n = 0-6$ , and  
 where R and R' are independently H, alkyl, heteroalkyl, aryl or heteroaryl;

$R_9$  is alkyl, aryl, heteroalkyl, or heteroaryl; and

$R_{10}$  and  $R_{11}$  are independently hydrogen, alkyl, aryl, heteroalkyl, electron  
 withdrawing group, F, Cl, CN,  $NO_2$ ,  $NR''R'''$ ,  $OR''$ ,  $SR''$ ,  $S(=O)R''$ ,  $SO_2R''$ ,  $C(=O)R''$ ,  
 10  $C(=O)OR''$ ,  $OC(=O)R''$ ,  $C(=O)NR''R'''$ ,  $N(R'')C(=O)R'''$ , or N-oxide group in the  
 pyrimidine nuclei, wherein R' and R''' are independently H, alkyl, heteroalkyl, aryl or  
 heteroaryl.

79. A compound of formula 11c, 12c or 13c:





## 13c

wherein:

$R_6$  is acyl or sulfonyl;

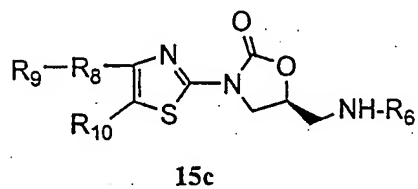
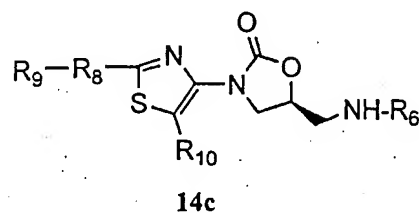
5  $R_8$  is  $C_1$ - $C_7$  alkyl, NR, O, S,  $C(=O)NR$ ,  $C(=O)NOR$ ,  $NRC(=O)$ ,  $C(=O)$ ,  $C(=O)O$ ,  $OC(=O)$ ,  $S(=O)$ ,  $SO_2$ ,  $SO_2NR$ ,  $NRSO_2$ ,  $NRCONR'$ , or  $(CH_2)_nO$ , wherein  $n = 0-6$ , and wherein R and R' are independently H, alkyl, heteroalkyl, aryl or heteroaryl;

$R_9$  is alkyl, aryl, heteroalkyl, or heteroaryl; and

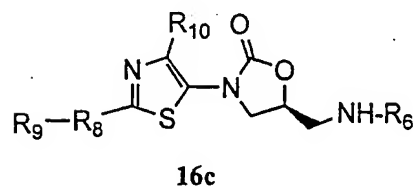
10  $R_{10}$  and  $R_{11}$  are independently hydrogen, alkyl, aryl, heteroalkyl, electron withdrawing group, F, Cl, CN,  $NO_2$ ,  $NR''R'''$ ,  $OR''$ ,  $SR''$ ,  $S(=O)R''$ ,  $SO_2R''$ ,  $C(=O)R''$ ,  $C(=O)OR''$ ,  $OC(=O)R''$ ,  $C(=O)NR''R'''$ , or  $N(R'')C(=O)R'''$ , wherein  $R''$  and  $R'''$  are independently H, alkyl, heteroalkyl, aryl or heteroaryl.

80. A compound of formula 14c, 15c or 16c:

15



20



wherein:

$R_6$  is acyl or sulfonyl;

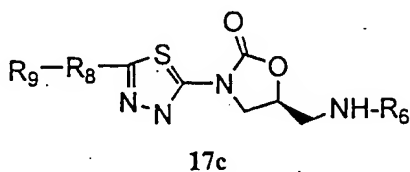
$R_8$  is  $C_1$ - $C_7$  alkyl, NR, O, S,  $C(=O)NR$ ,  $C(=O)NOR$ ,  $NRC(=O)$ ,  $C(=O)$ ,  $C(=O)O$ ,  $OC(=O)$ ,  $S(=O)$ ,  $SO_2$ ,  $SO_2NR$ ,  $NRSO_2$ ,  $NRCONR'$ , or  $(CH_2)_nO$ , wherein  $n = 0-6$ , and

5 wherein R and R' are independently H, alkyl, heteroalkyl, aryl or heteroaryl;

$R_9$  is alkyl, aryl, heteroalkyl, or heteroaryl; and

$R_{10}$  is hydrogen, alkyl, aryl, heteroalkyl, electron withdrawing group, F, Cl, CN,  $NO_2$ ,  $NR''R'''$ ,  $OR''$ ,  $SR''$ ,  $S(=O)R''$ ,  $SO_2R''$ ,  $C(=O)R''$ ,  $C(=O)OR''$ ,  $OC(=O)R''$ ,  $C(=O)NR''R'''$ , or  $N(R'')C(=O)R'''$ , where  $R''$  and  $R'''$  are independently H, alkyl, heteroalkyl, aryl or heteroaryl.

81. A compound of formula 17c:



wherein:

$R_6$  is acyl or sulfonyl;

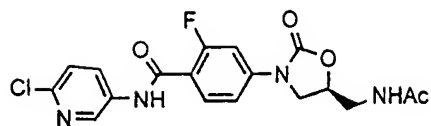
$R_8$  is  $C_1$ - $C_7$  alkyl, NR, O, S,  $C(=O)NR$ ,  $C(=O)NOR$ ,  $NRC(=O)$ ,  $C(=O)$ ,  $C(=O)O$ ,  $OC(=O)$ ,  $S(=O)$ ,  $SO_2$ ,  $SO_2NR$ ,  $NRSO_2$ ,  $NRCONR'$ , or  $(CH_2)_nO$ , where  $n = 0-6$ , and

20 where R and R' are independently H, alkyl, heteroalkyl, aryl or heteroaryl; and

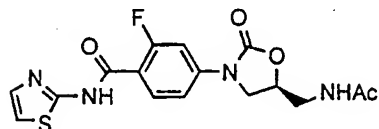
$R_9$  is alkyl, aryl, heteroalkyl, or heteroaryl.

82. A composition for the treatment or prevention of an infectious disorder comprising an effective amount of a compound of claim 14 and a pharmaceutically acceptable carrier.

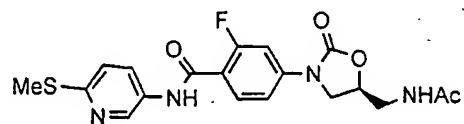
83. The composition of claim 82 wherein the compound is



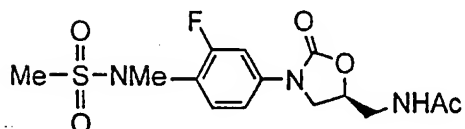
84. The composition of claim 82 wherein the compound is



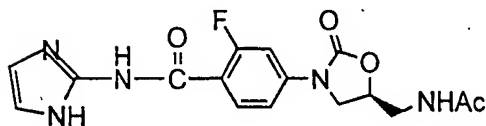
85. The composition of claim 82 wherein the compound is



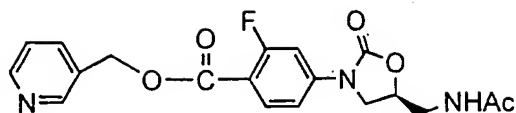
86. The composition of claim 82 wherein the compound is



87. The composition of claim 82 wherein the compound is



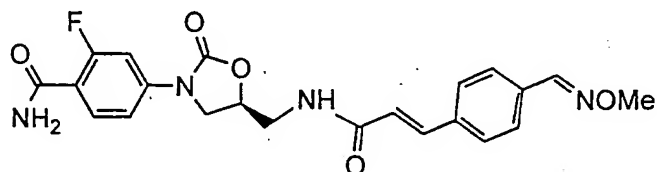
88. The composition of claim 82 wherein the compound is



89. A composition for the treatment or prevention of an infectious disorder comprising an effective amount of a compound of claim 55 and a pharmaceutically acceptable carrier.

90. A composition for the treatment or prevention of an infectious disorder comprising an effective amount of a compound of claim 57 and a pharmaceutically acceptable carrier.

91. The composition of claim 82, wherein the compound is



92. A composition for the treatment or prevention of an infectious disorder comprising an effective amount of a compound of claim 61 and a pharmaceutically acceptable carrier.

93. A composition for the treatment or prevention of an infectious disorder comprising an effective amount of a compound of claim 64 and a pharmaceutically acceptable carrier.

94. A composition for the treatment or prevention of an infectious disorder comprising an effective amount of a compound of claim 72 and a pharmaceutically acceptable carrier.

95. A method of treating or preventing an infectious disorder in a human or other animal subject, comprising administering to the subject an effective amount of a compound of claim 14.

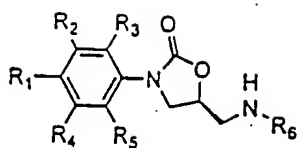
5 96. A method of treating or preventing an infectious disorder in a human or other animal subject, comprising administering to the subject an effective amount of a compound of claim 55.

10 97. A method of treating or preventing an infectious disorder in a human or other animal subject, comprising administering to the subject an effective amount of a compound of claim 57.

15 98. A method of treating or preventing an infectious disorder in a human or other animal subject, comprising administering to the subject an effective amount of a compound of claim 61.

20 99. A method of treating or preventing an infectious disorder in a human or other animal subject, comprising administering to the subject an effective amount of a compound of claim 64.

100. A method of treating or preventing an infectious disorder in a human or other animal subject, comprising administering to the subject an effective amount of a compound of claim 72.



1b

FIGURE 1

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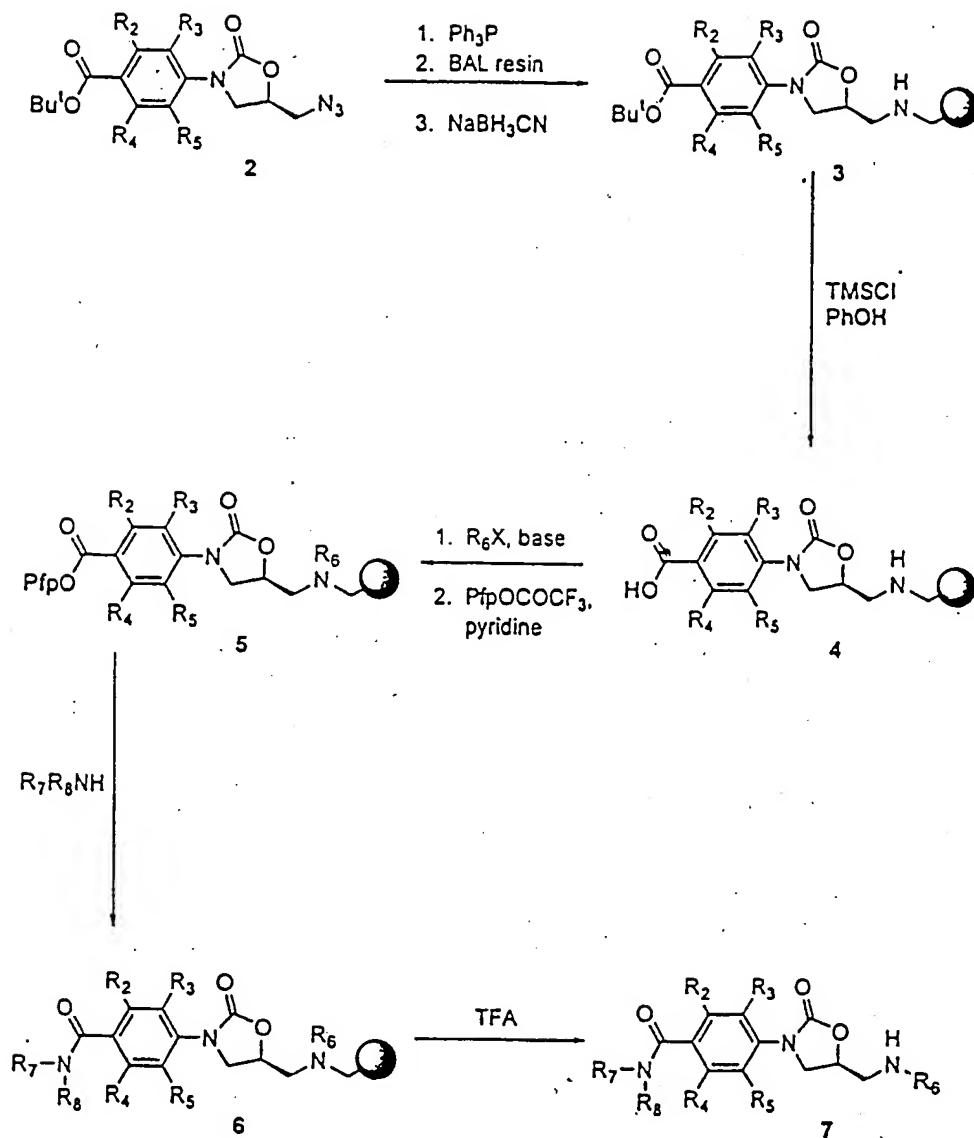


FIGURE 2

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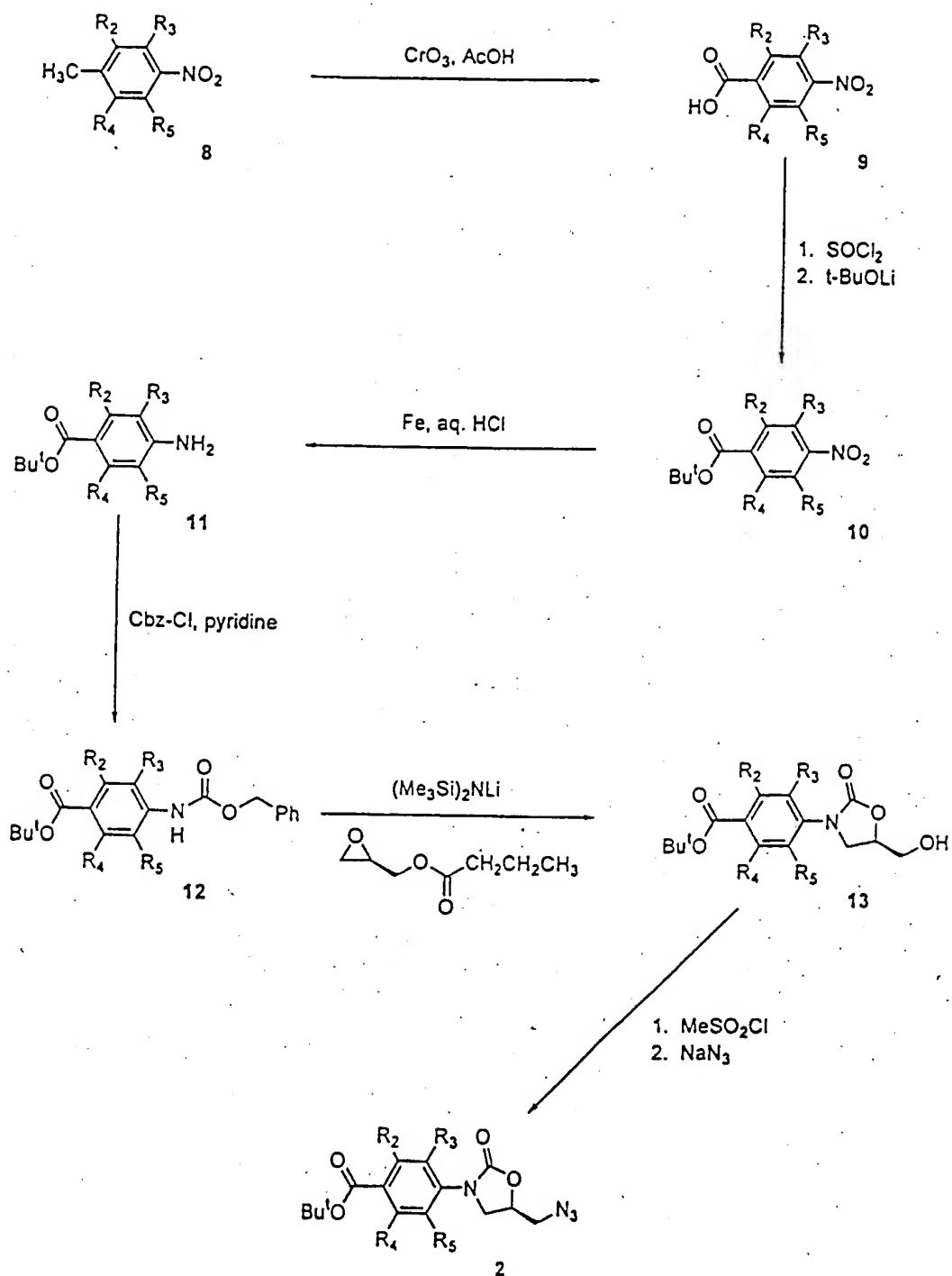


FIGURE 3



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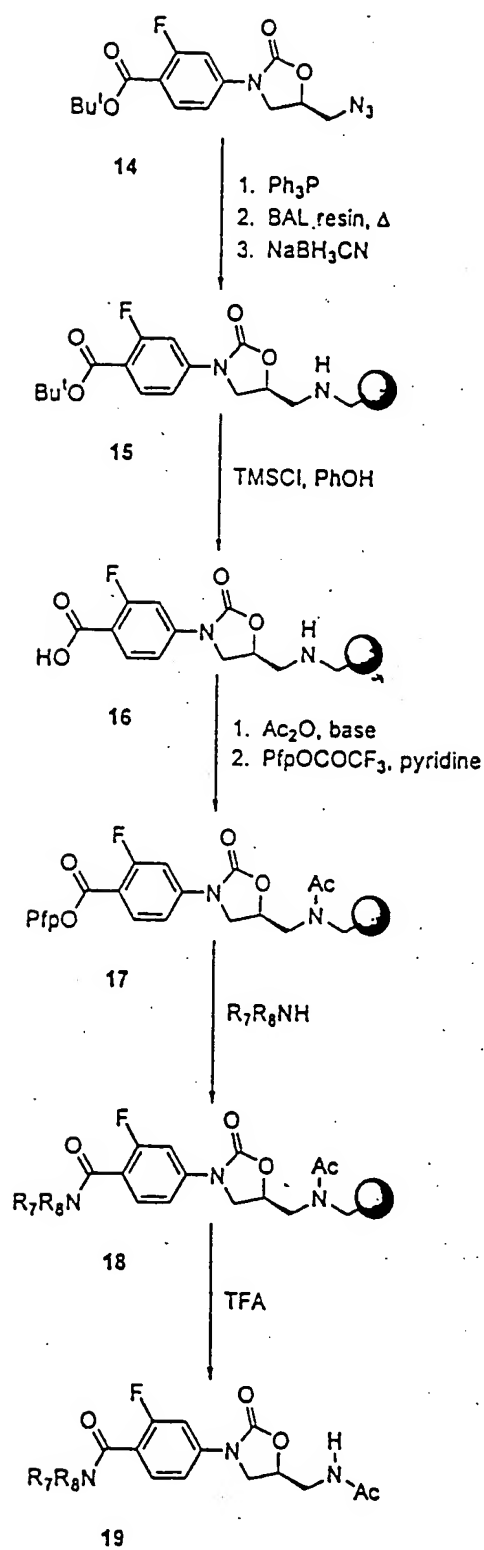


FIGURE 4

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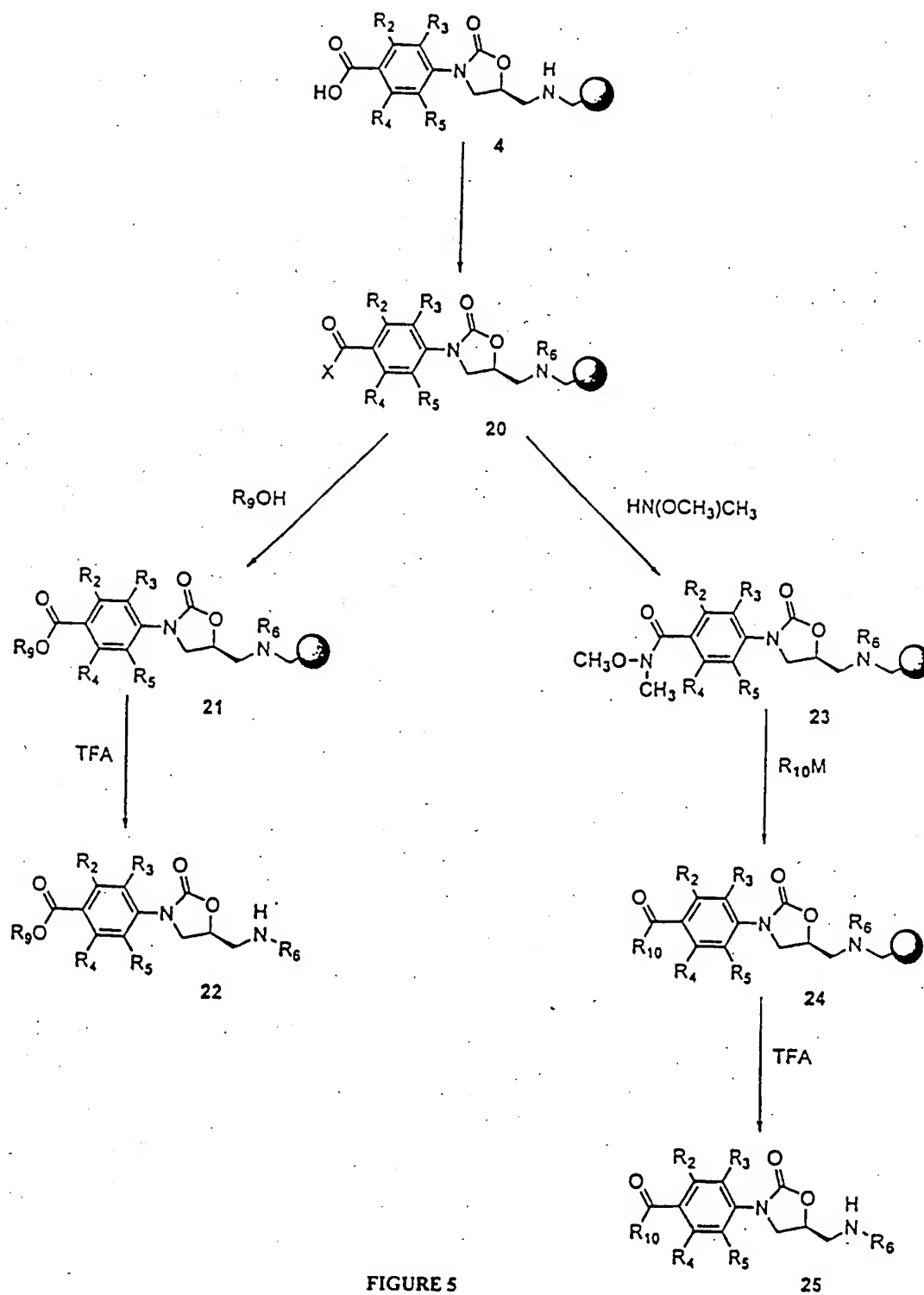


FIGURE 5

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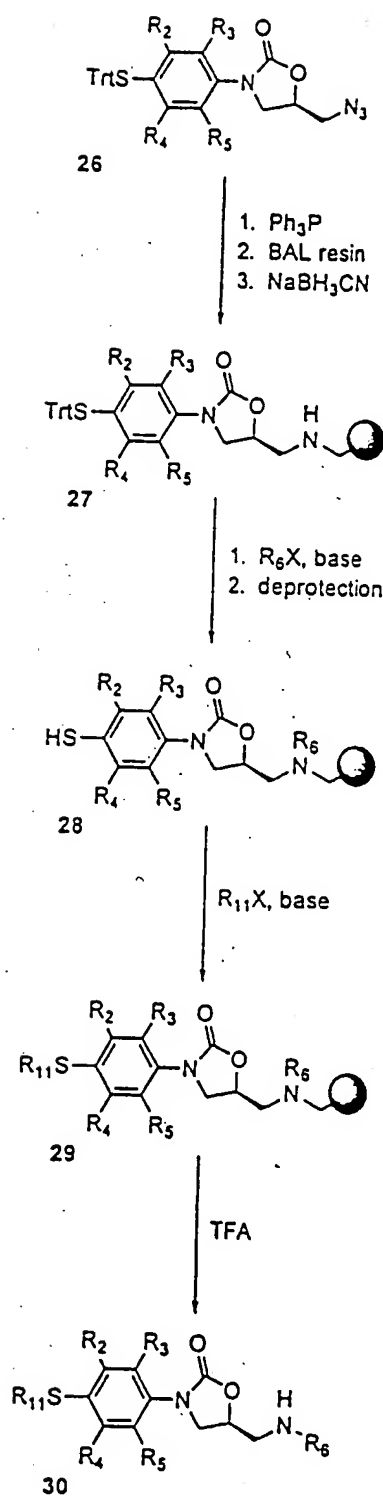


FIGURE 6

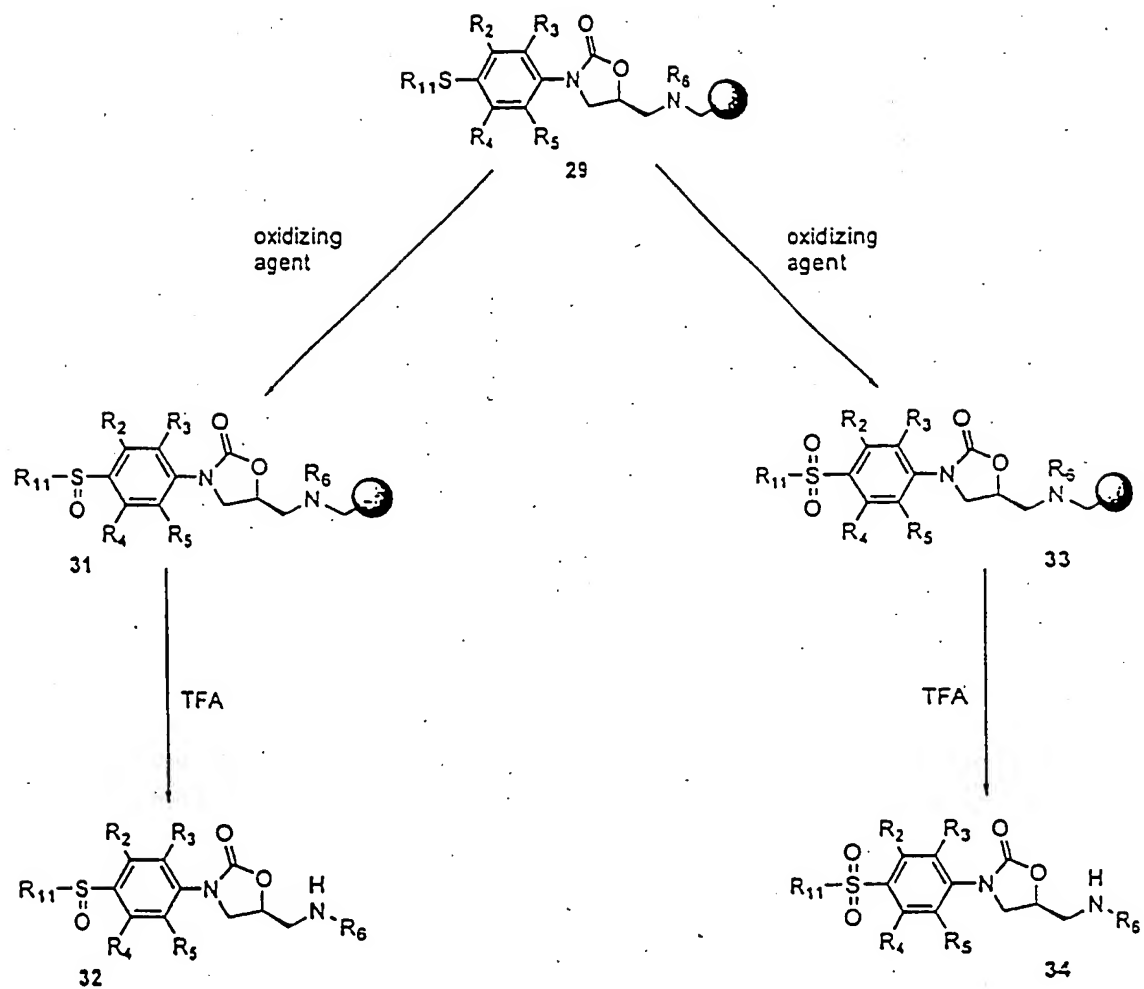


FIGURE 7

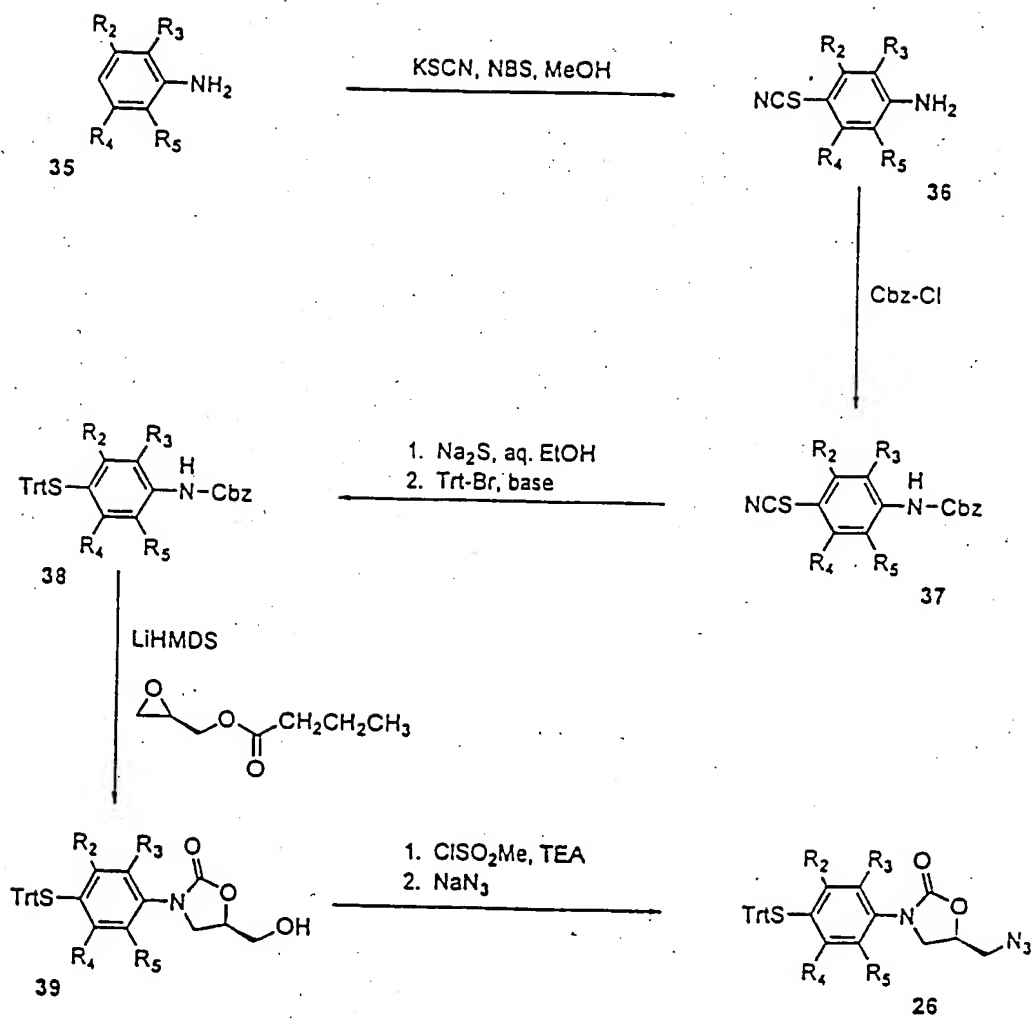


FIGURE 8

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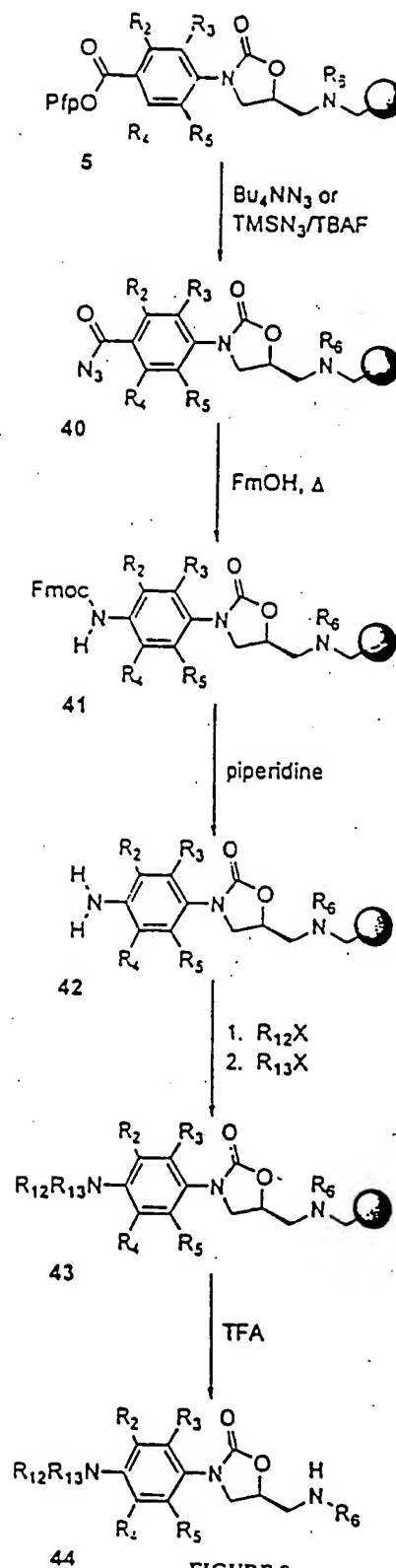


FIGURE 9

10 / 50

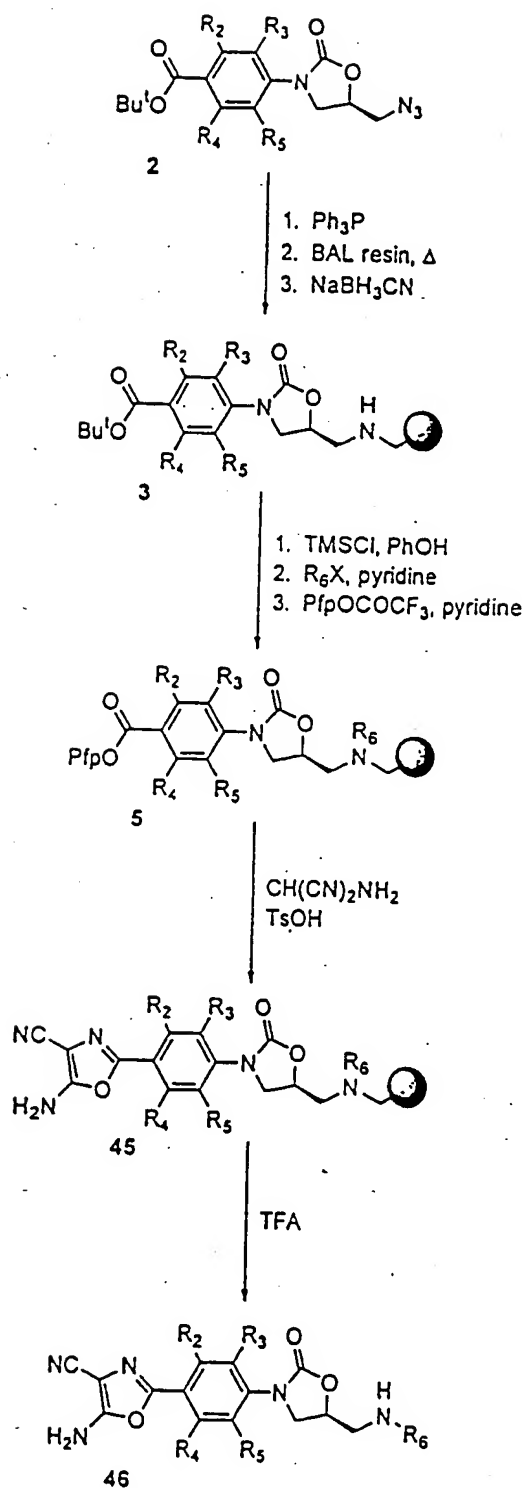


FIGURE 10

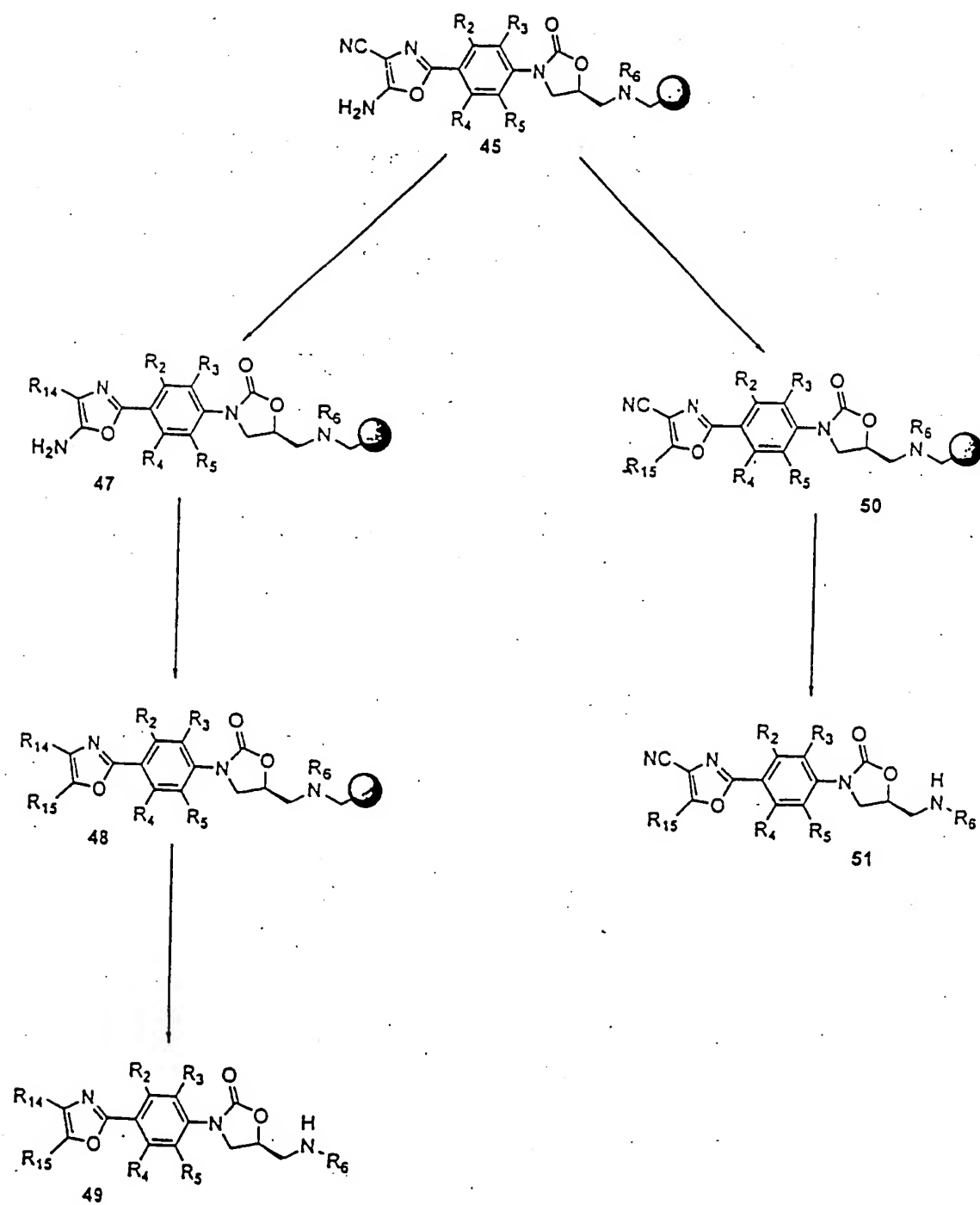


FIGURE 11



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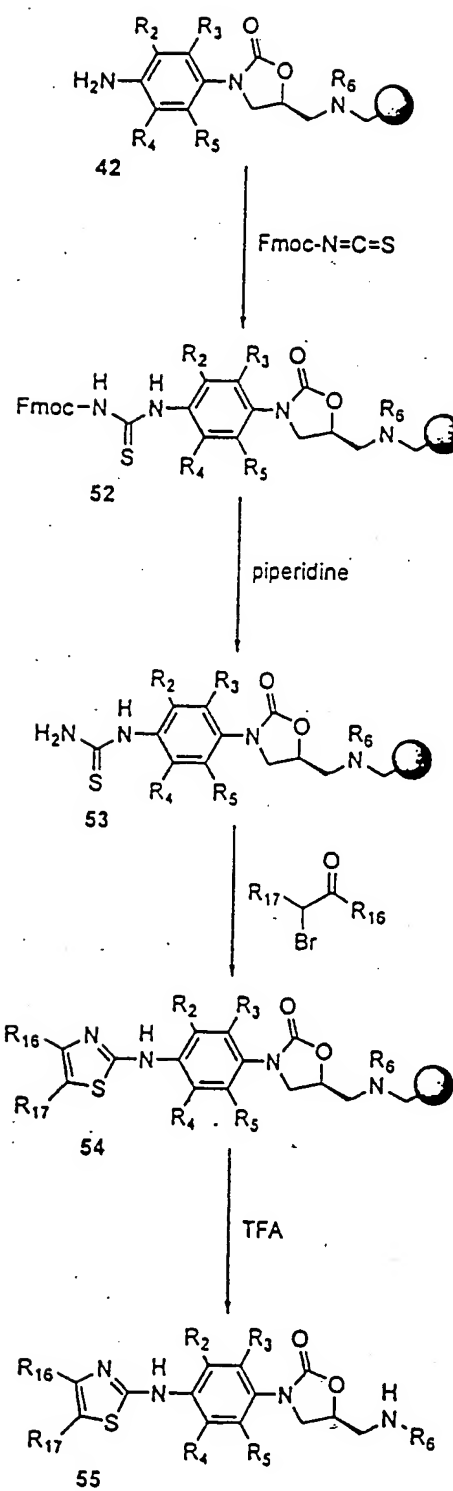


FIGURE 12

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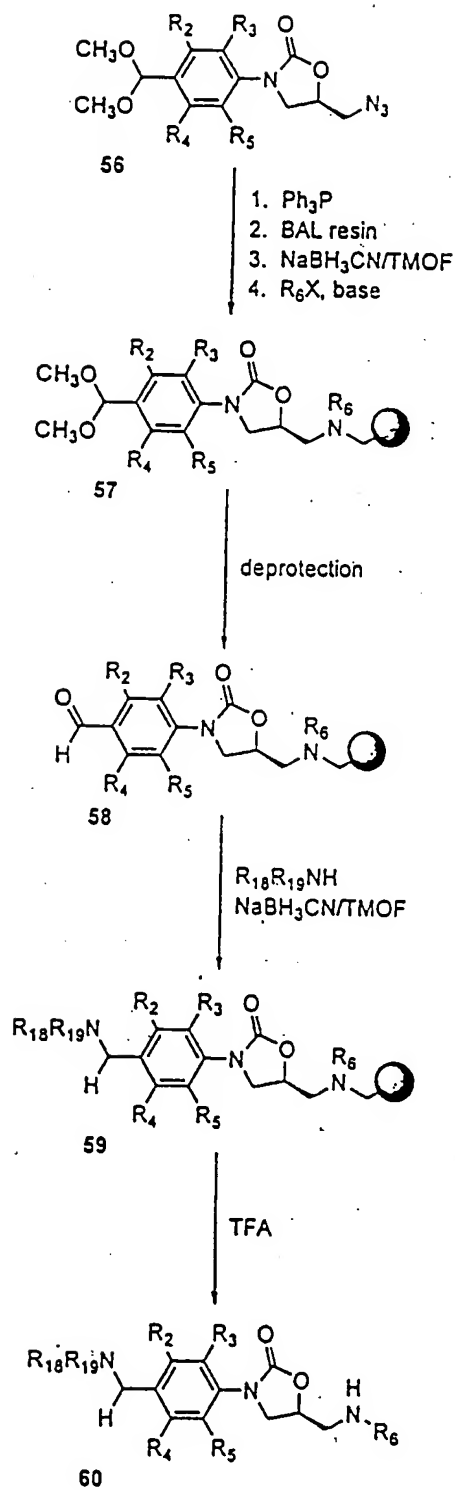


FIGURE 13

14 / 50

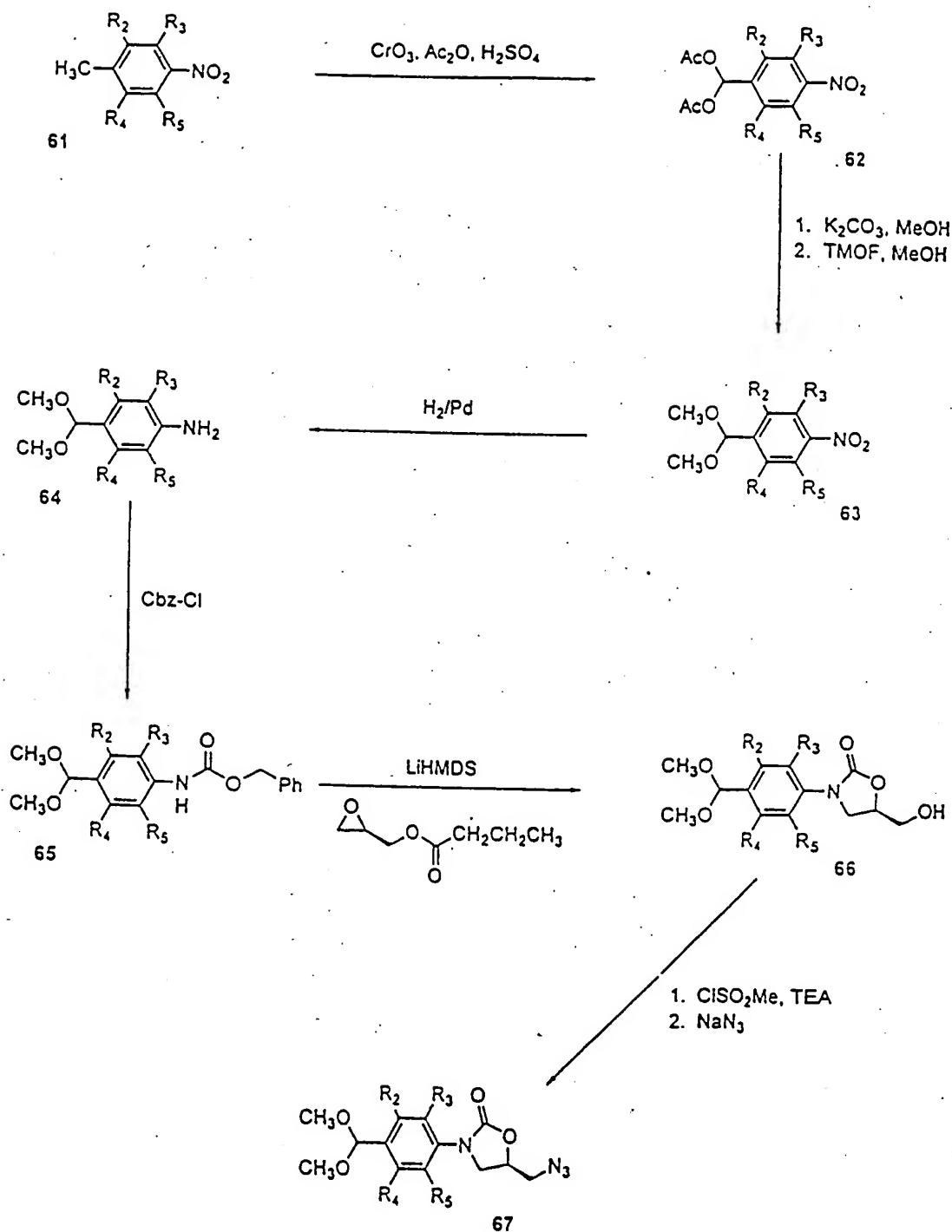


FIGURE 14

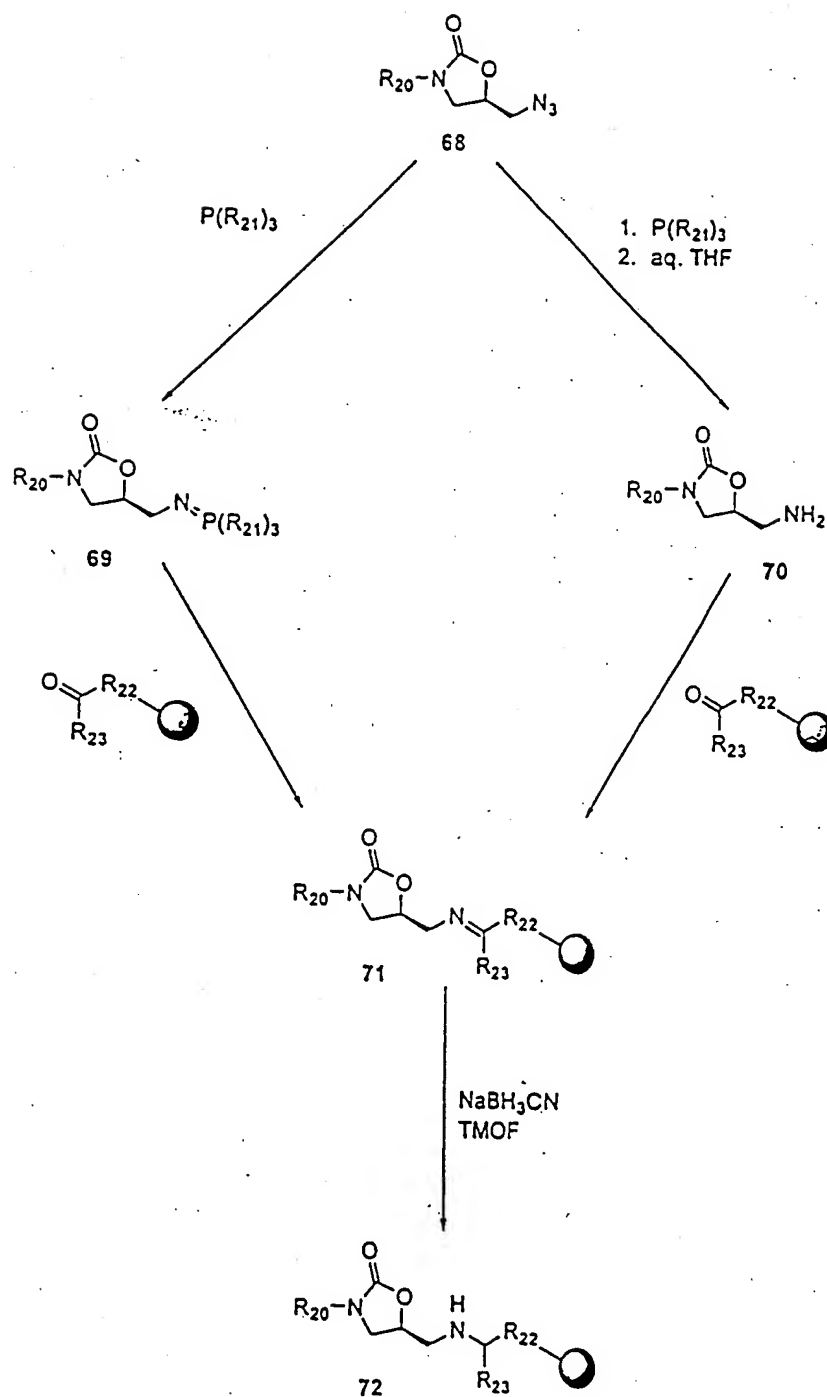


FIGURE 15

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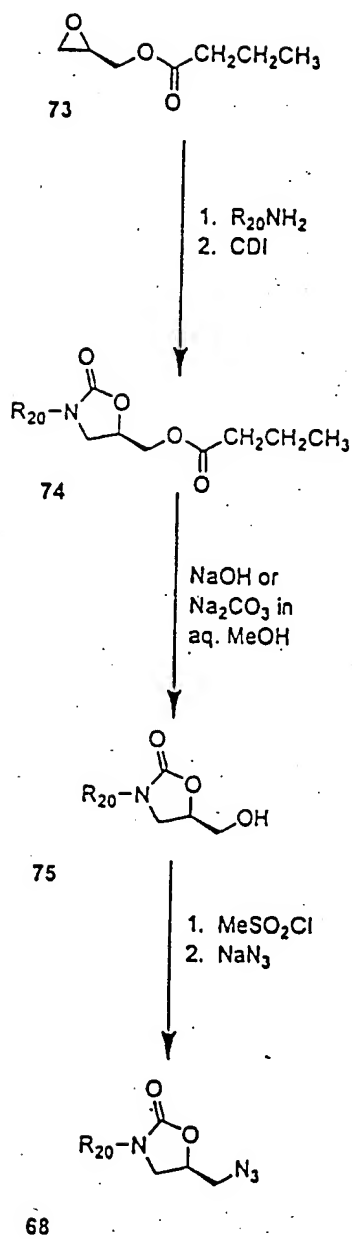


FIGURE 16

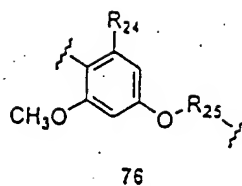


FIGURE 17

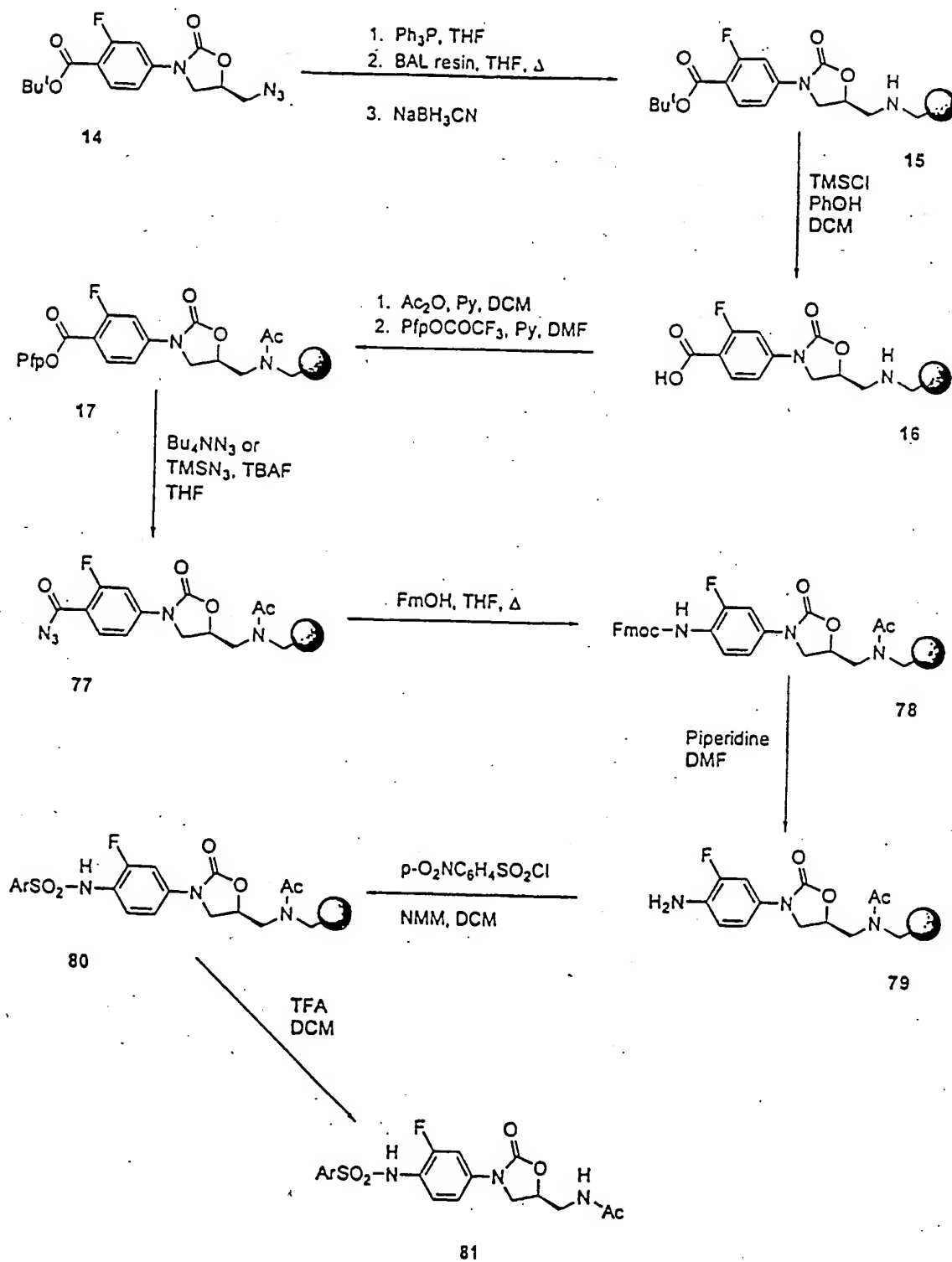


FIGURE 18

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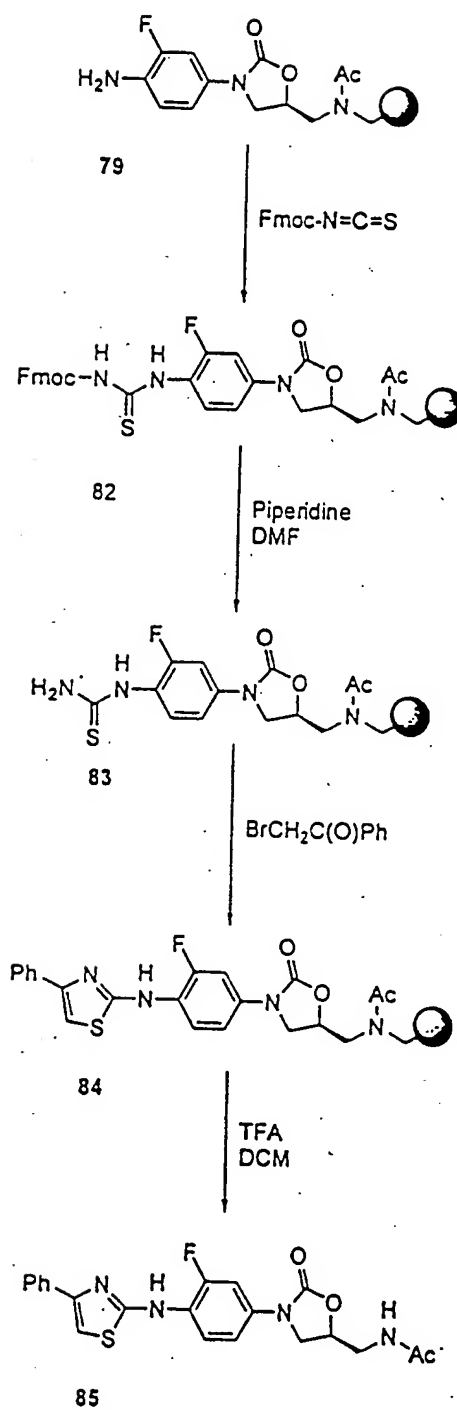


FIGURE 19



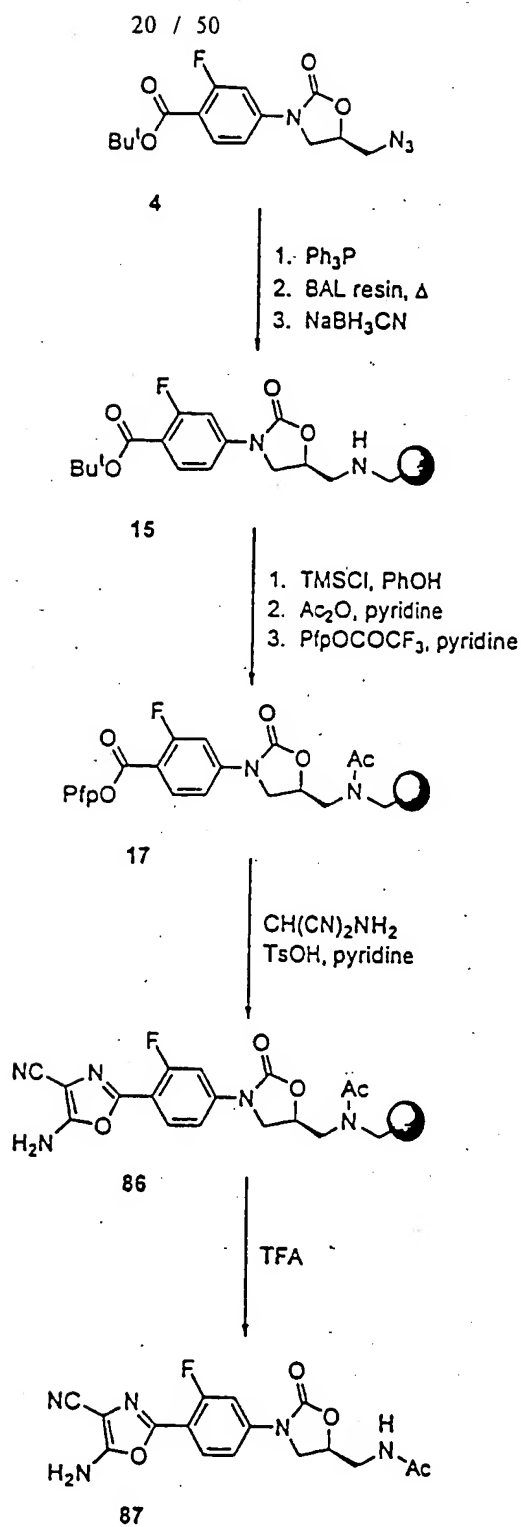


FIGURE 20

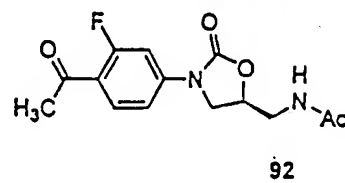
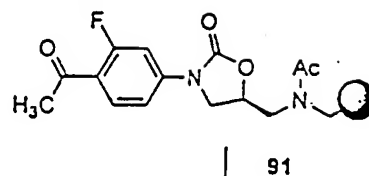
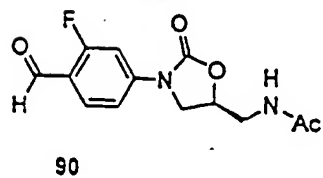
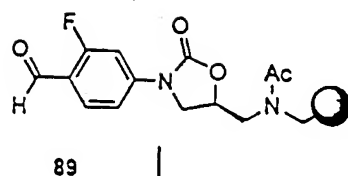
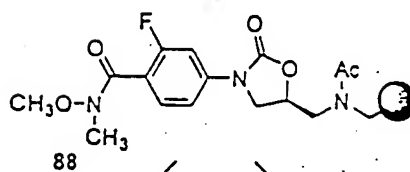
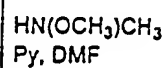


FIGURE 21

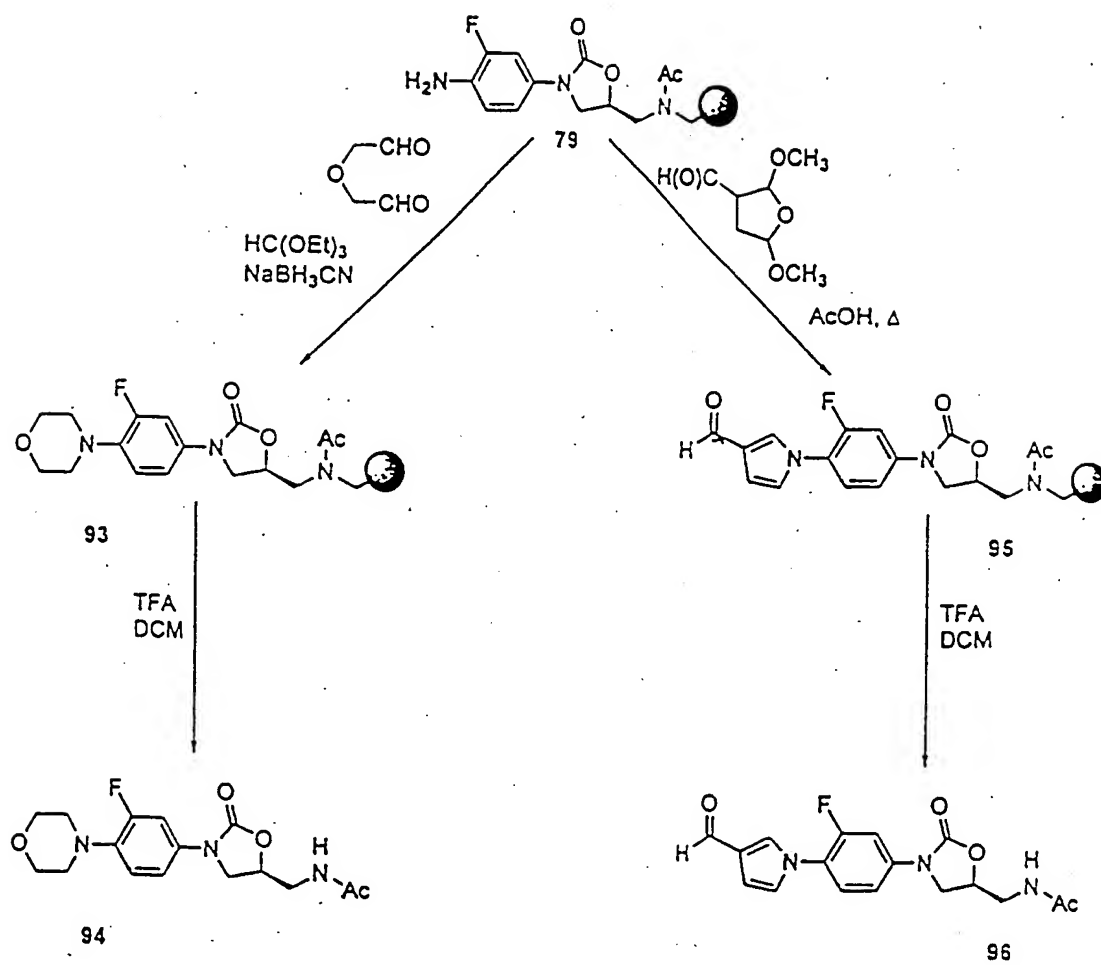


FIGURE 22

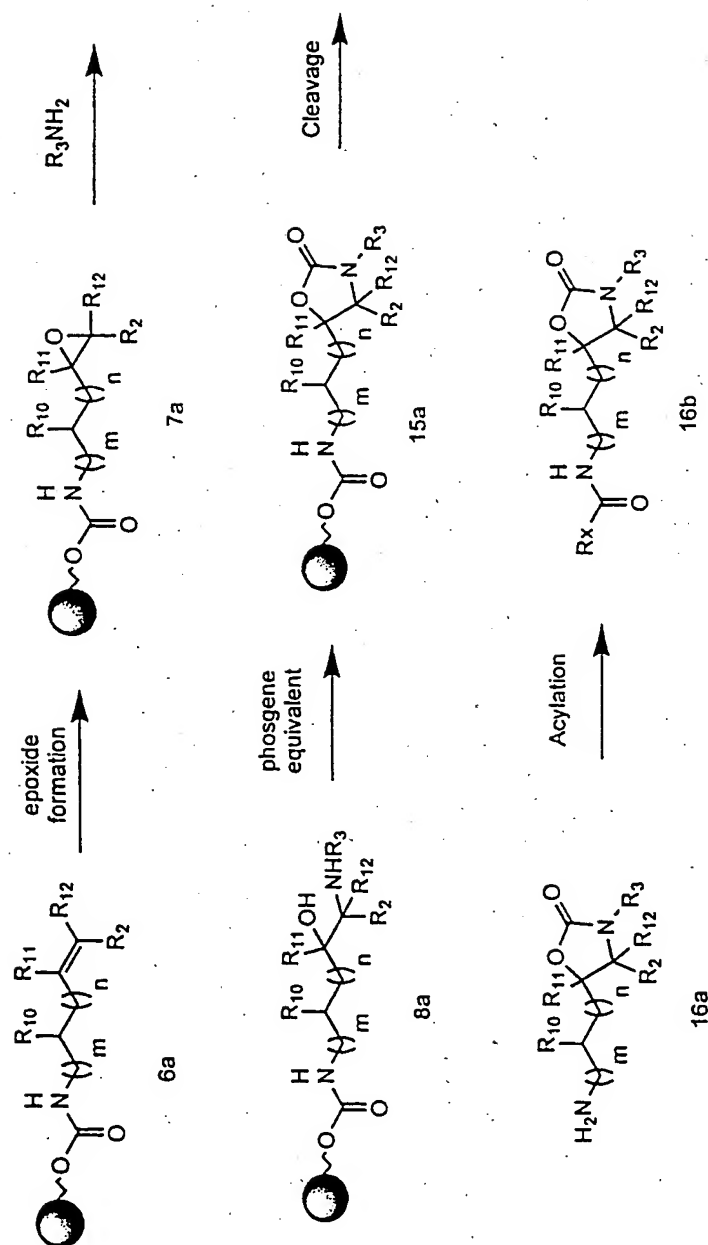


FIGURE 23

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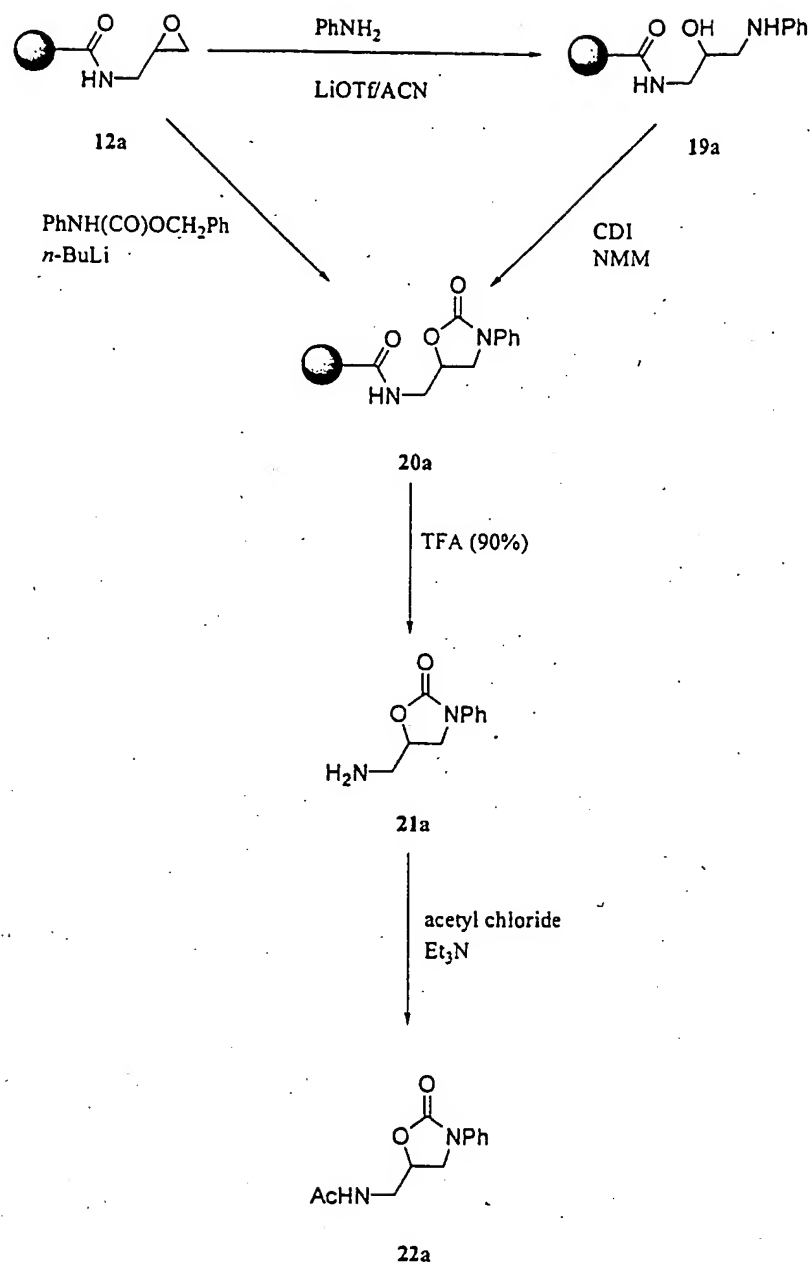


FIGURE 24

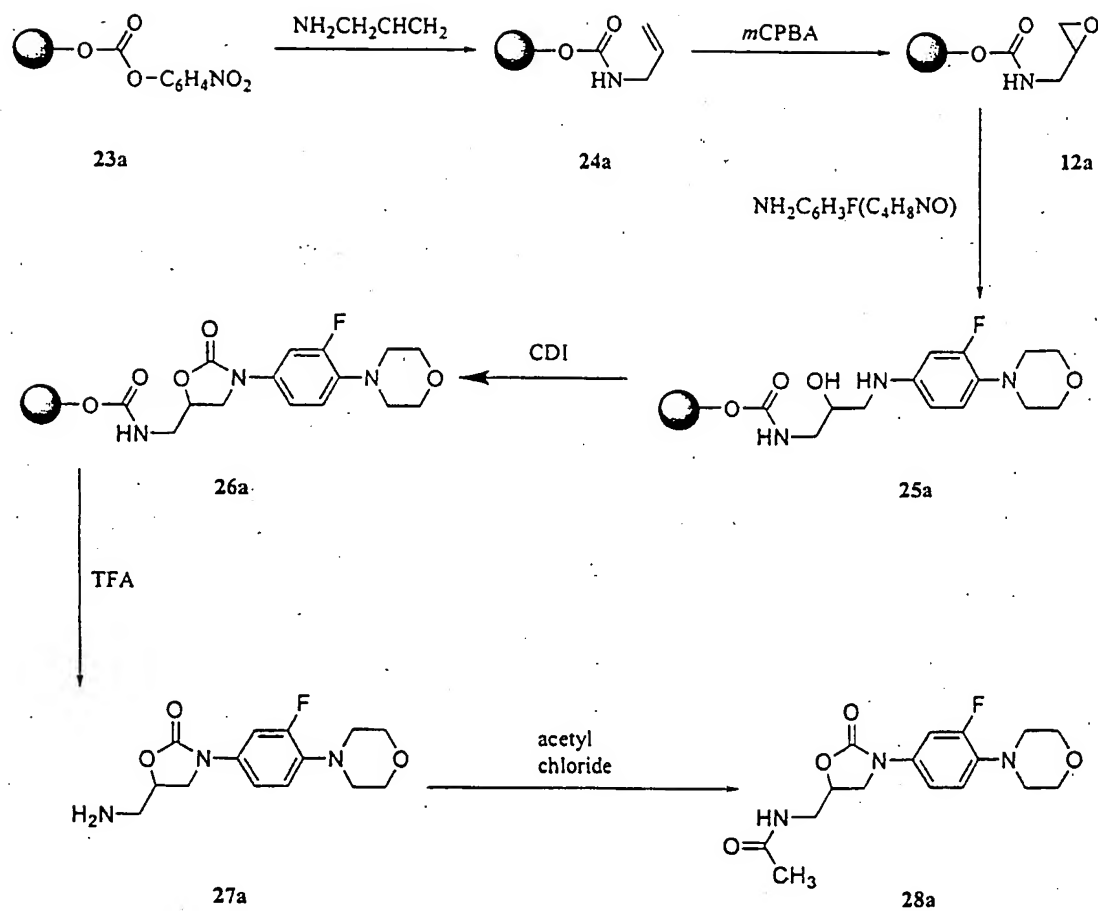


FIGURE 25

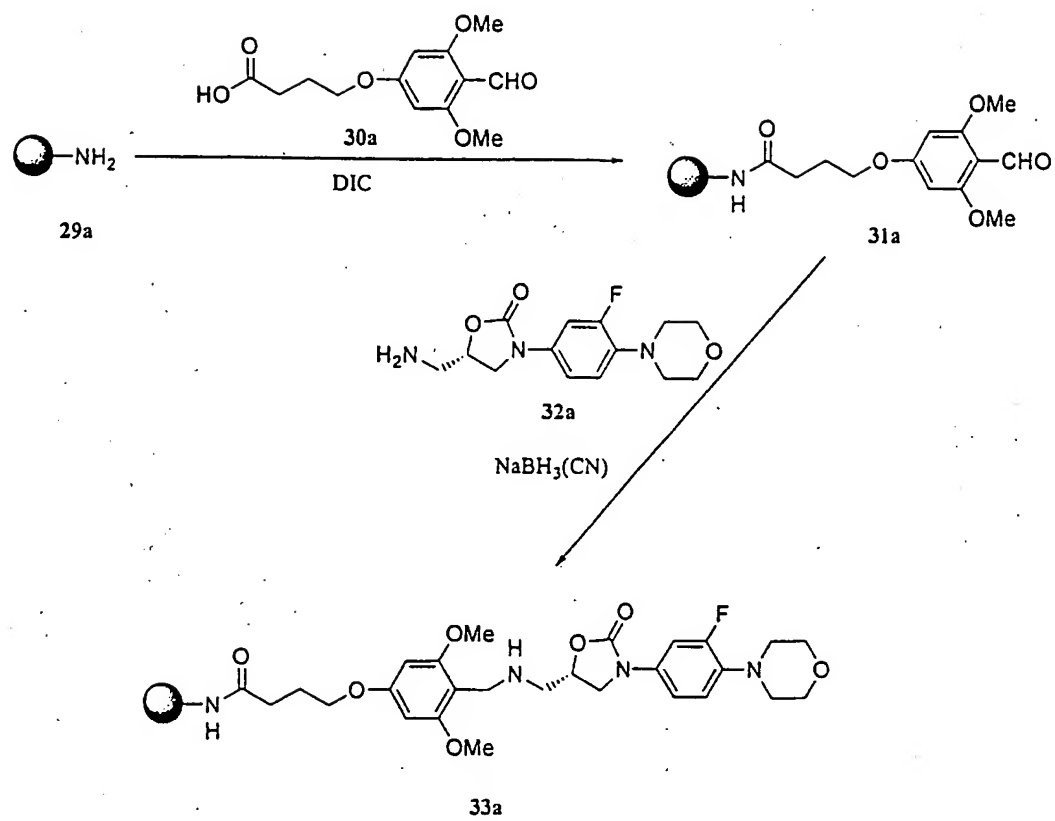


FIGURE 26

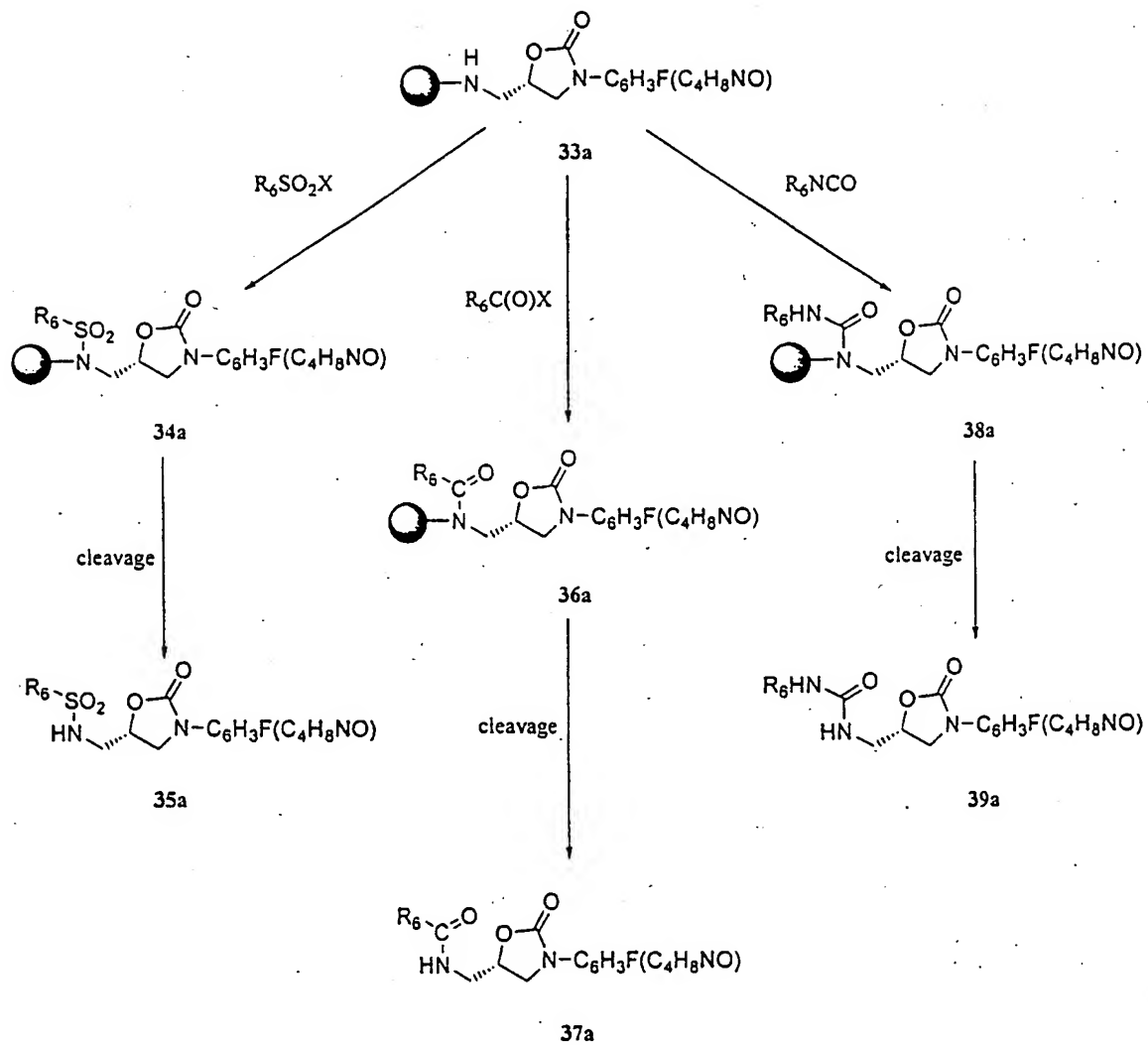


FIGURE 27



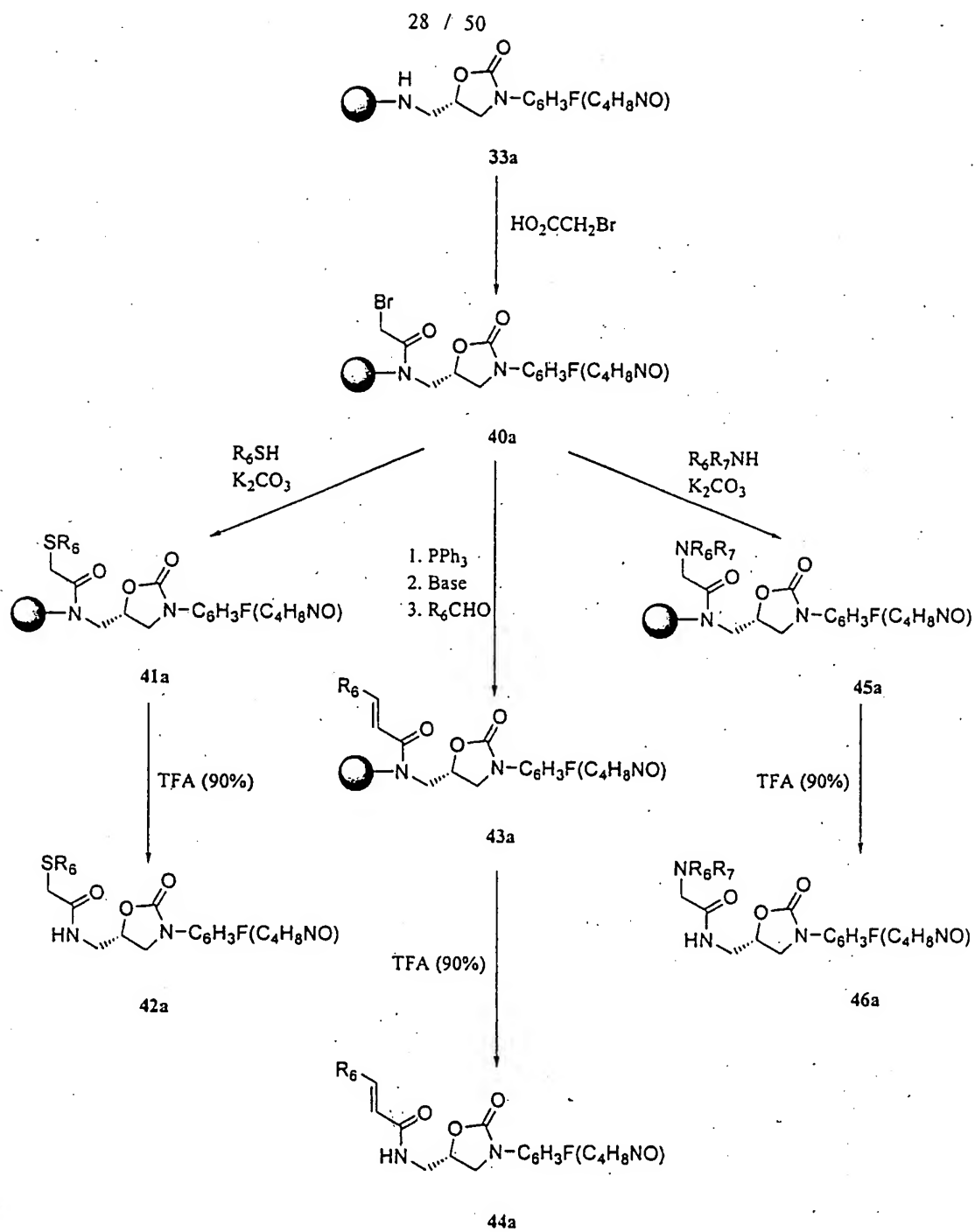


FIGURE 28

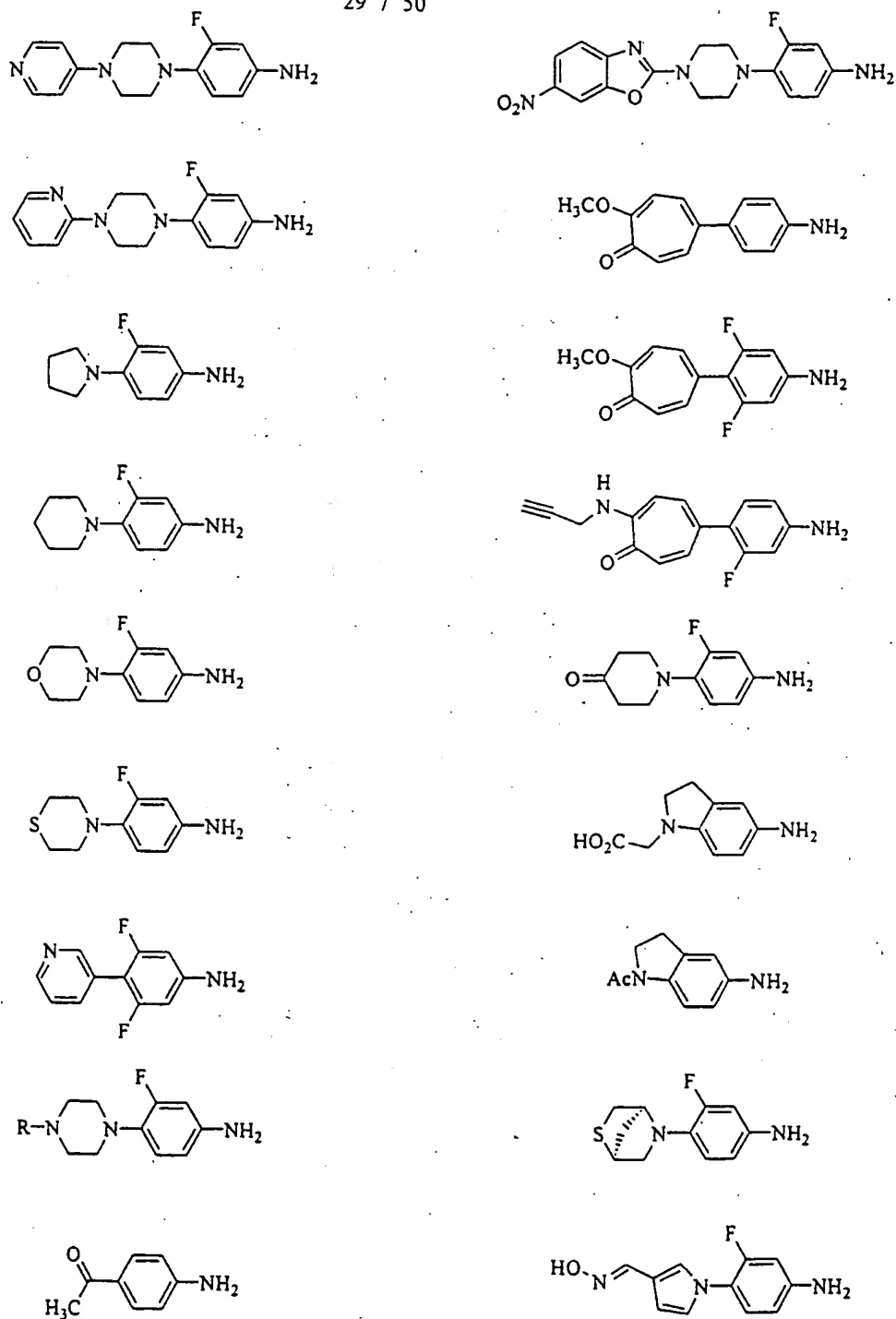


FIGURE 29

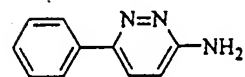
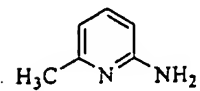
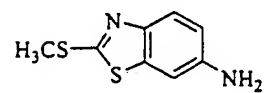
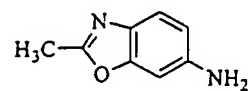
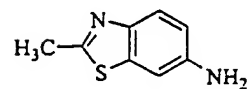
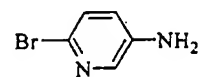
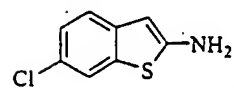
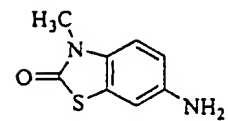
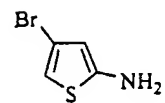
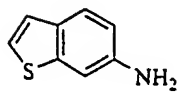
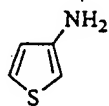
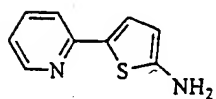
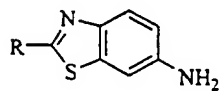
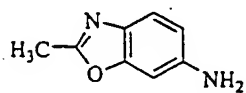
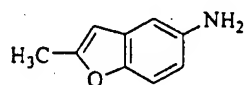
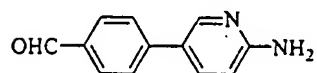
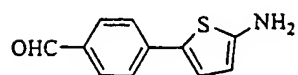
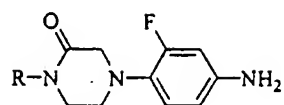


FIGURE 30

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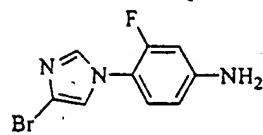
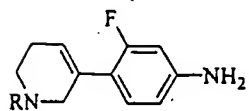
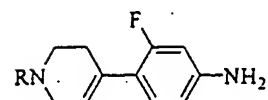
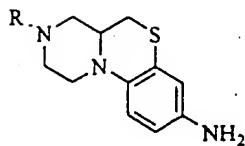
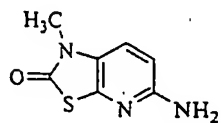
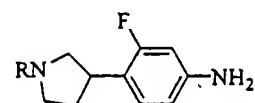
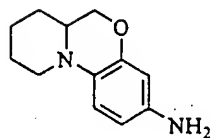
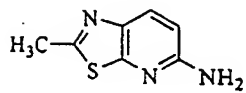
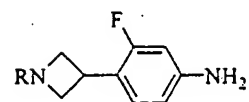
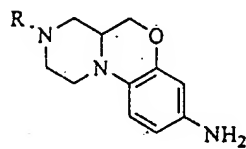
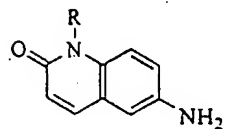
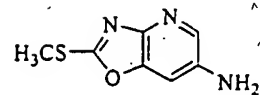
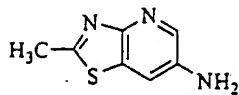
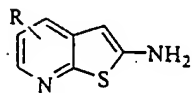
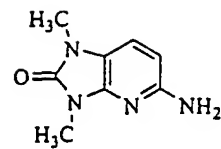
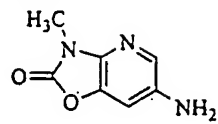
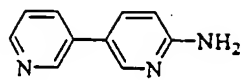


FIGURE 31

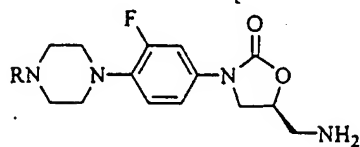
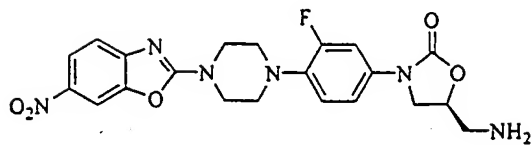
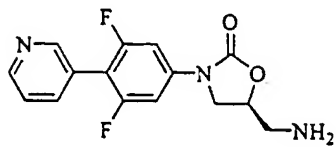
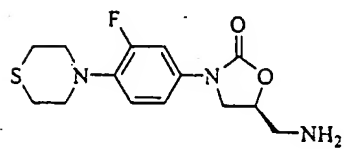
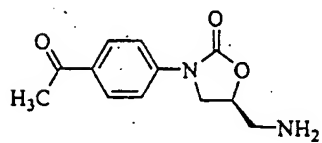
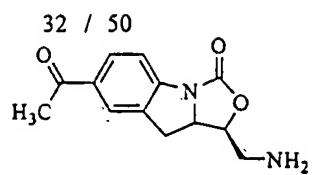


FIGURE 32

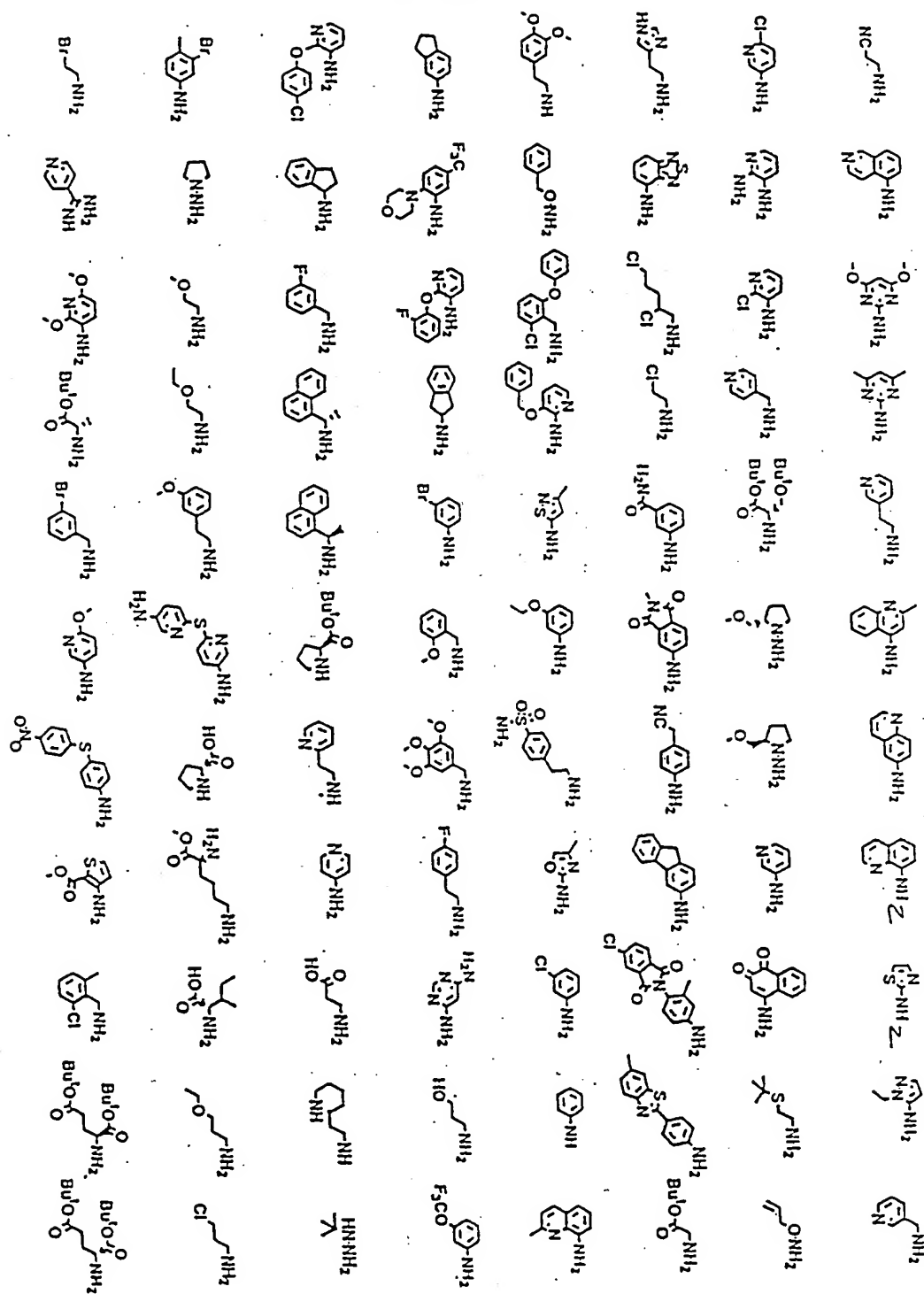


FIGURE 33

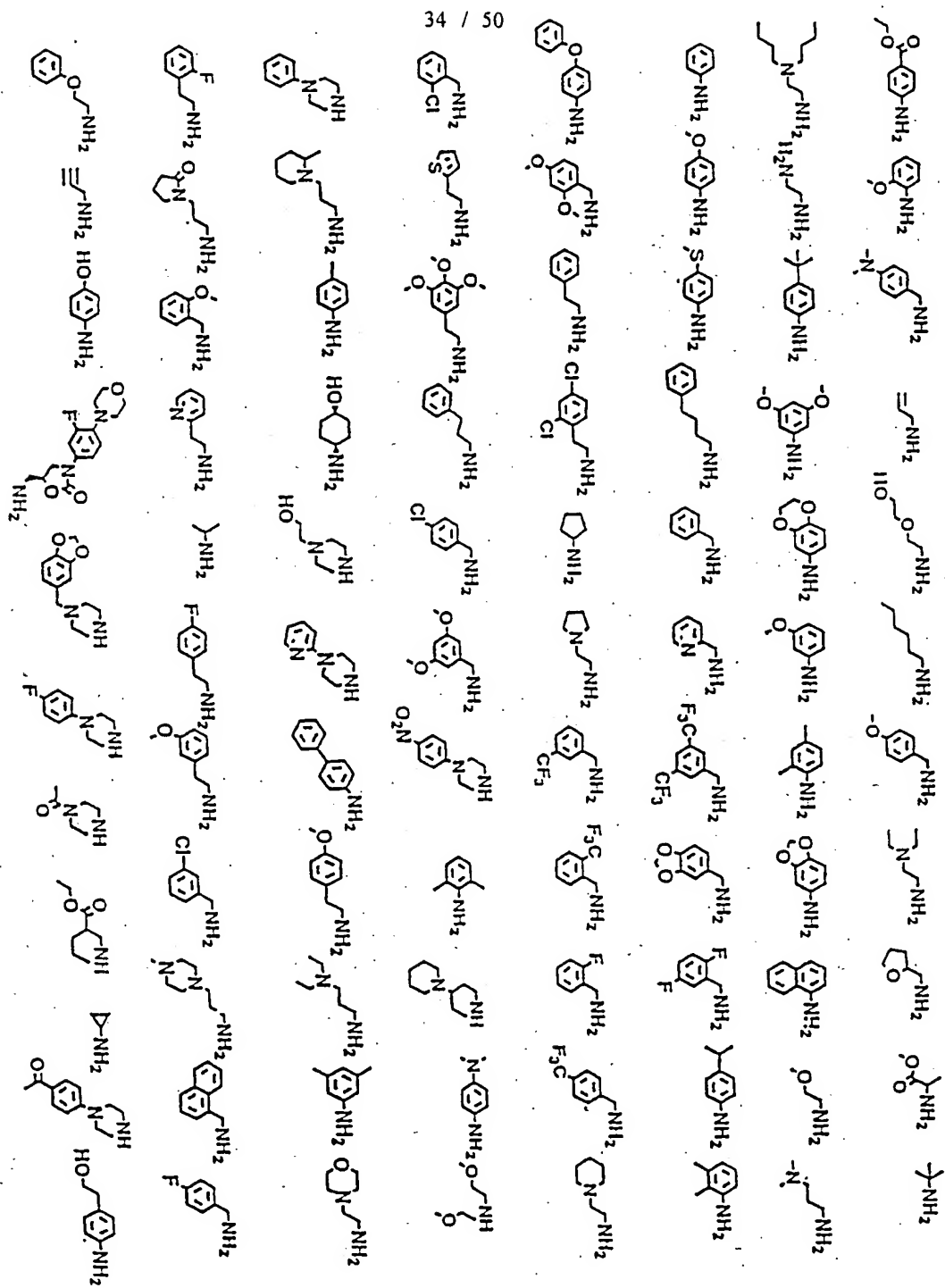


FIGURE 34

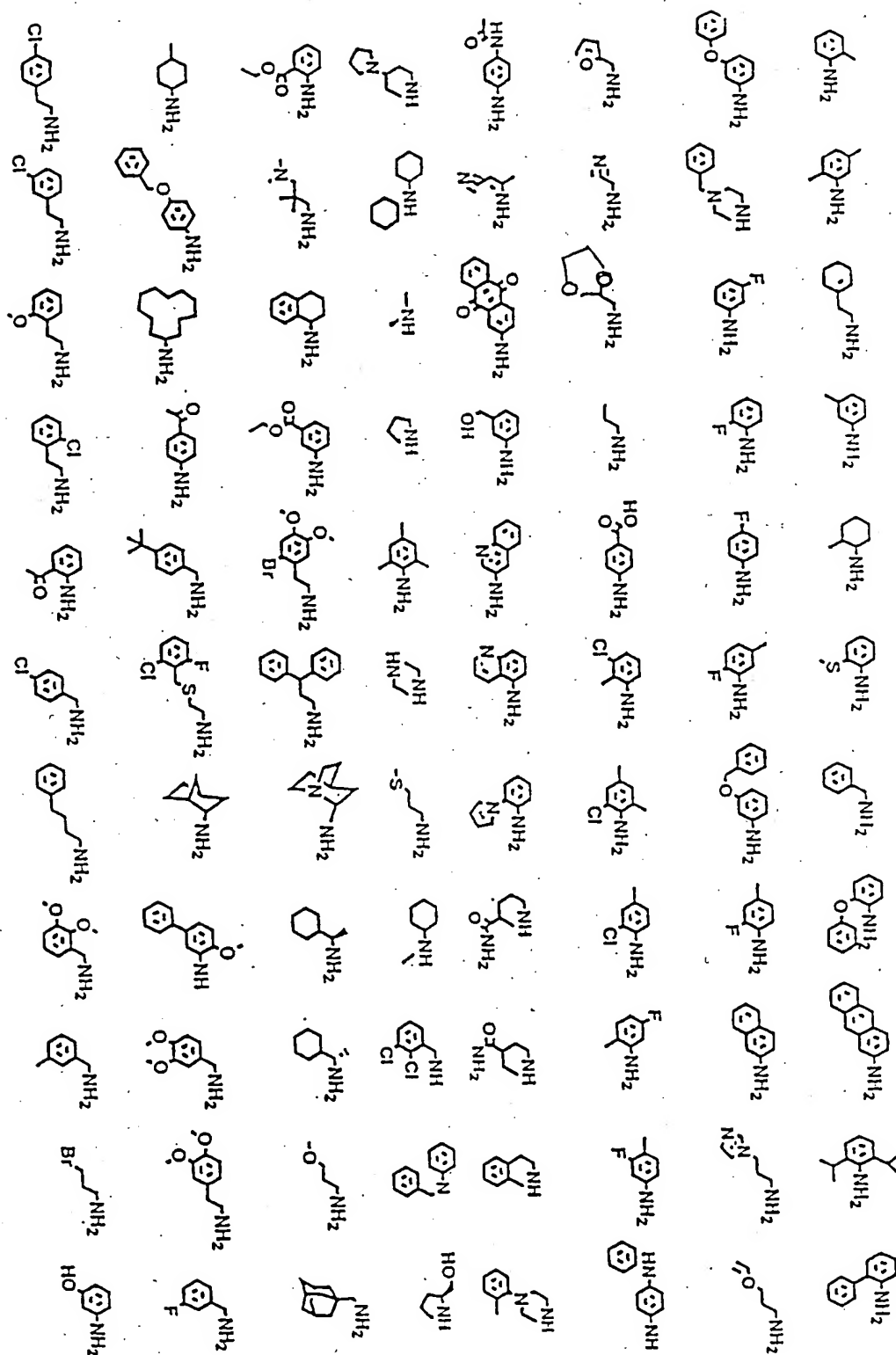


FIGURE 35



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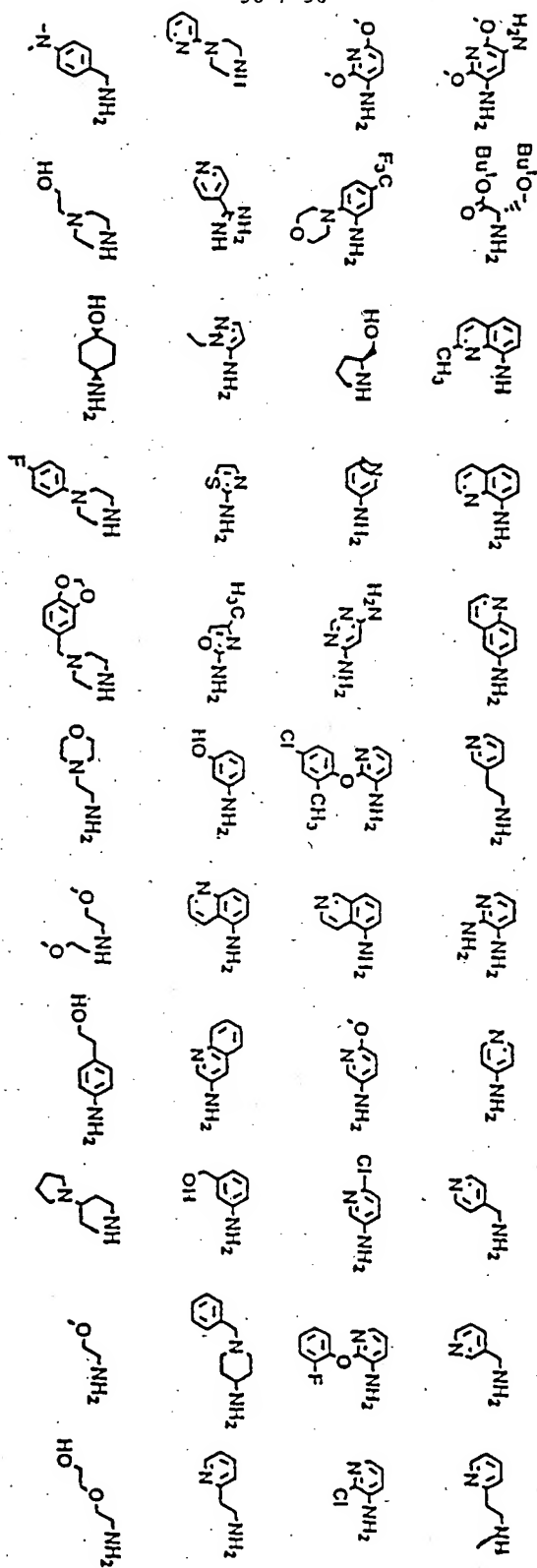


FIGURE 36

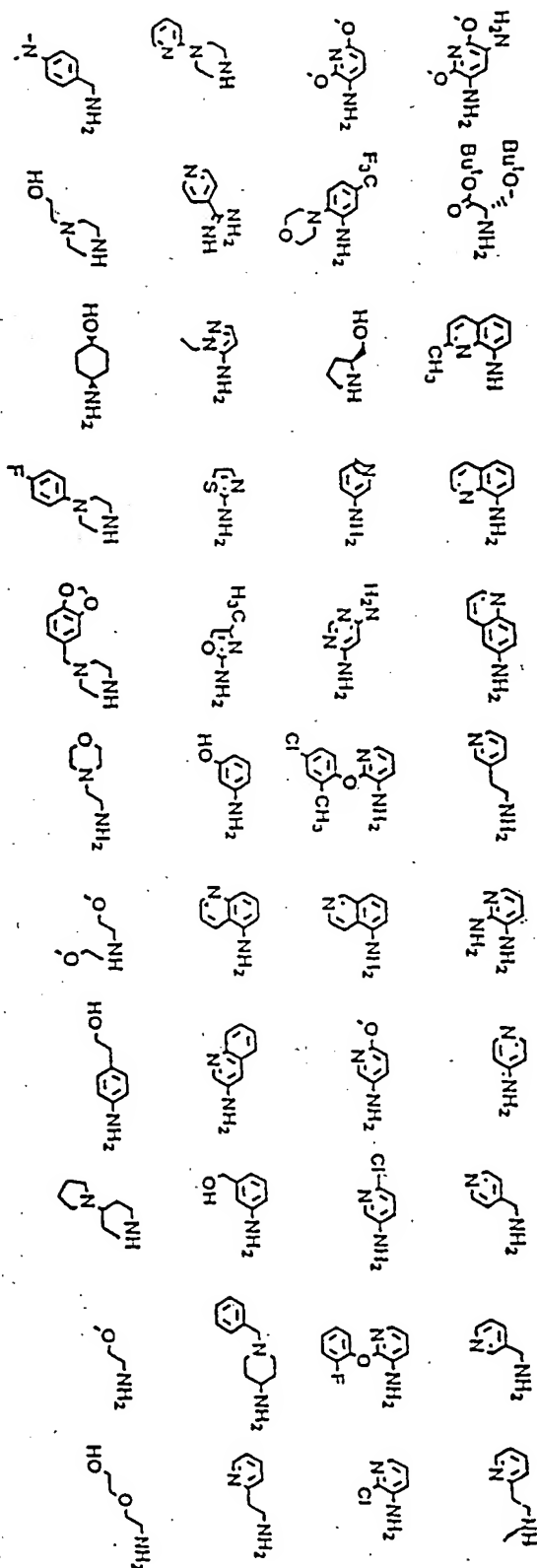


FIGURE 37

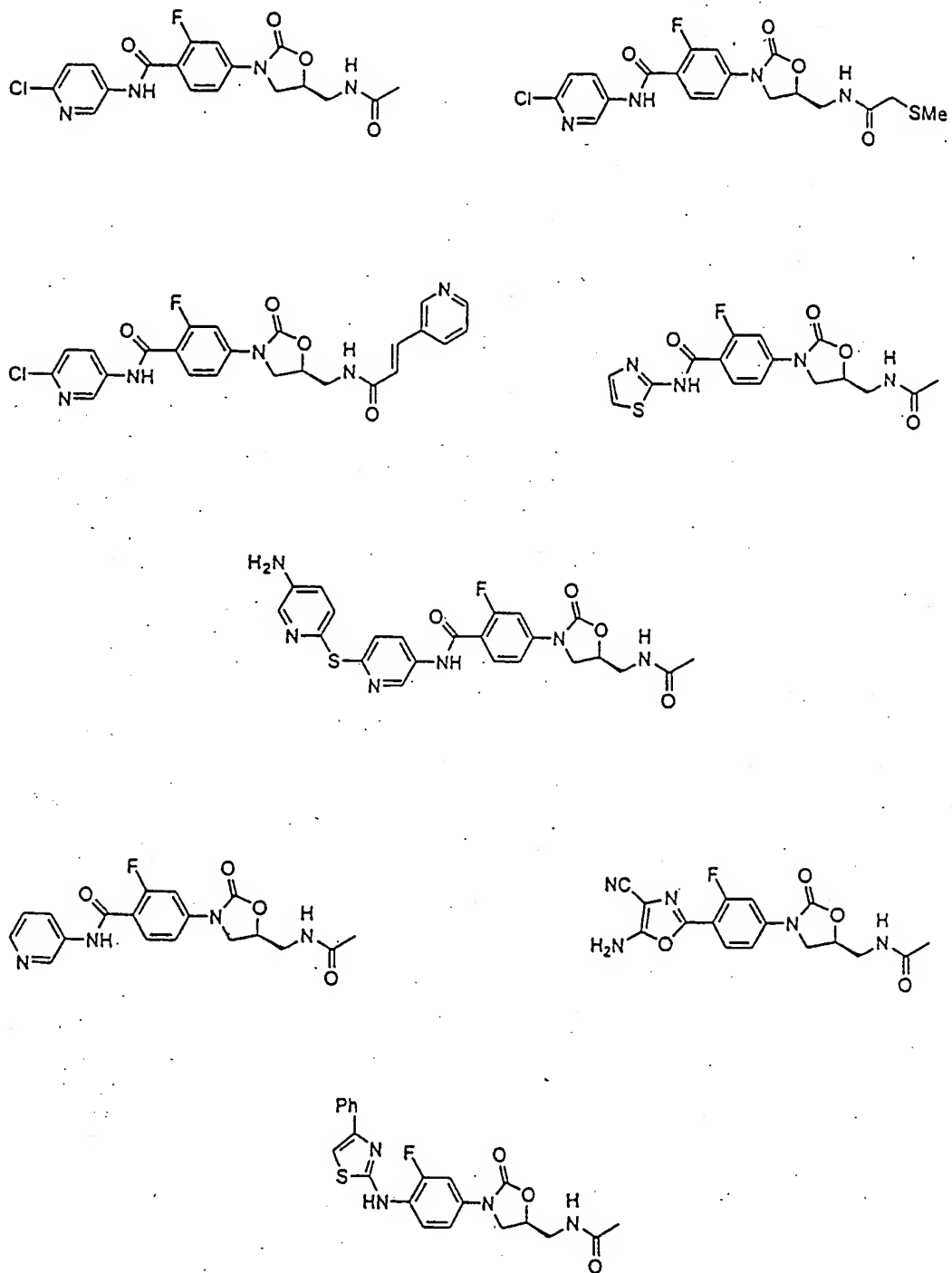


FIGURE 38

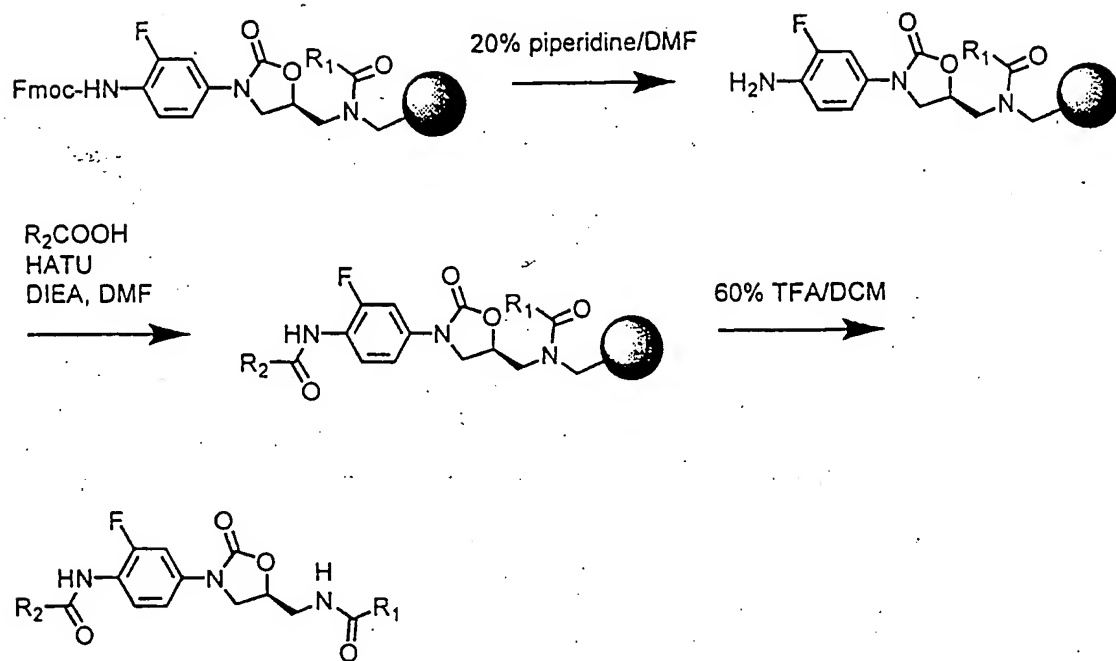


FIGURE 39

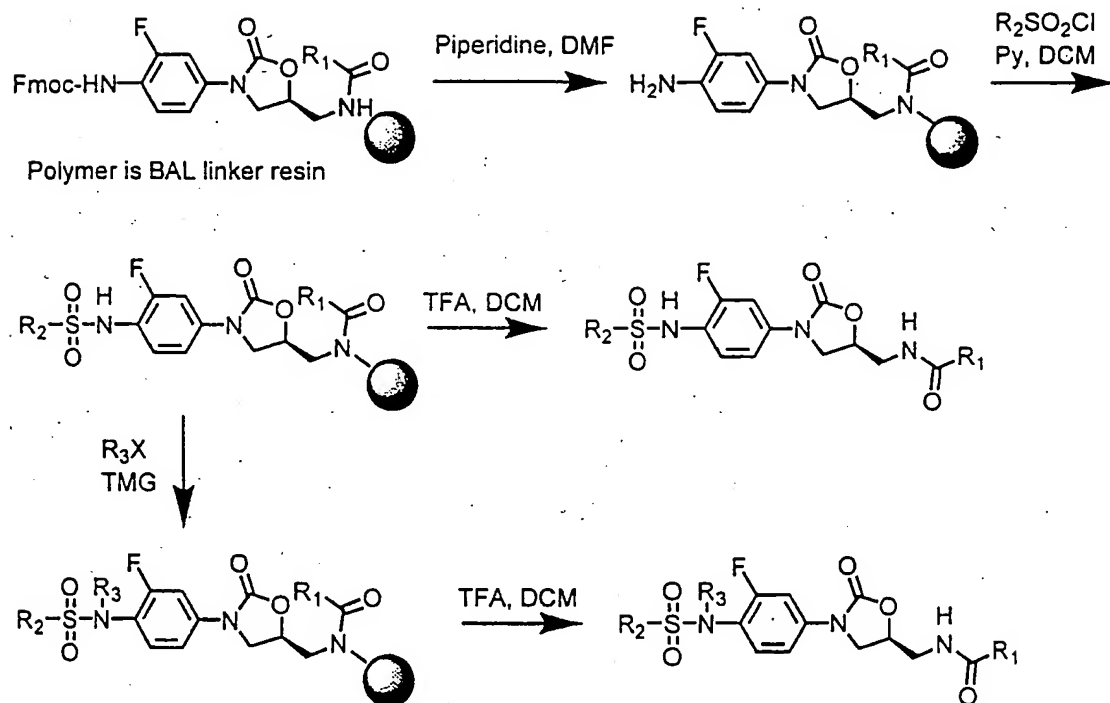


FIGURE 40

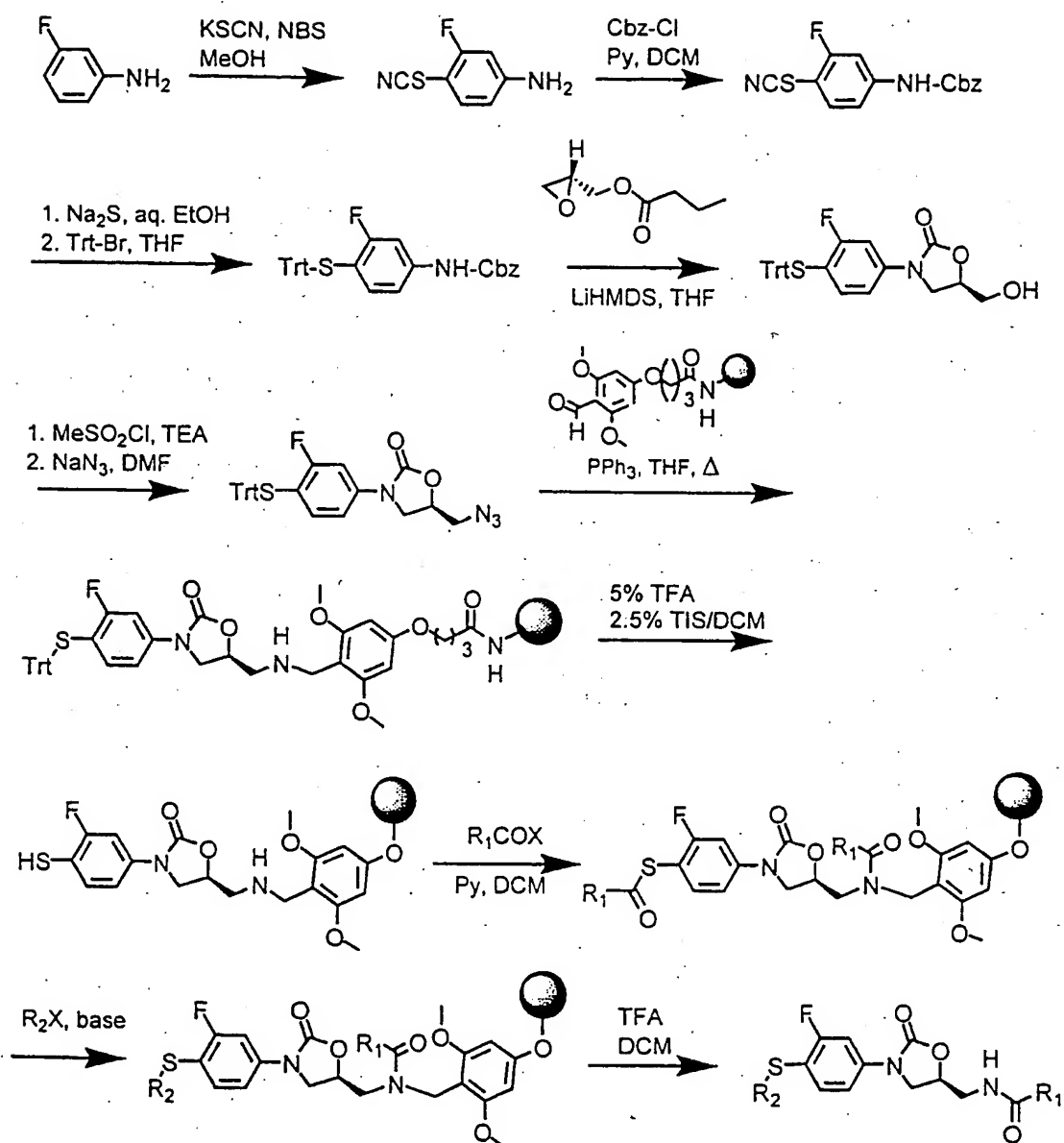


FIGURE 41

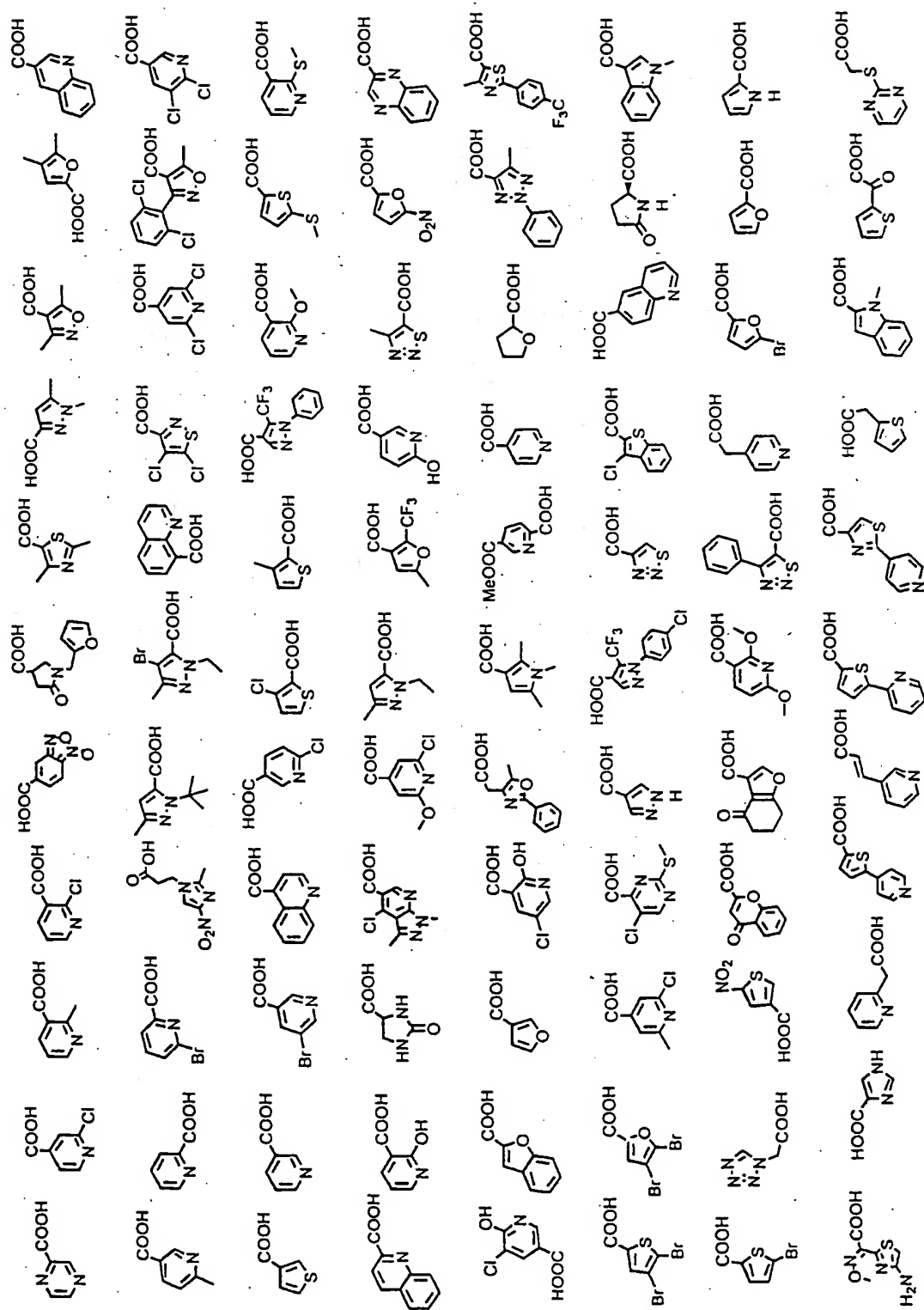
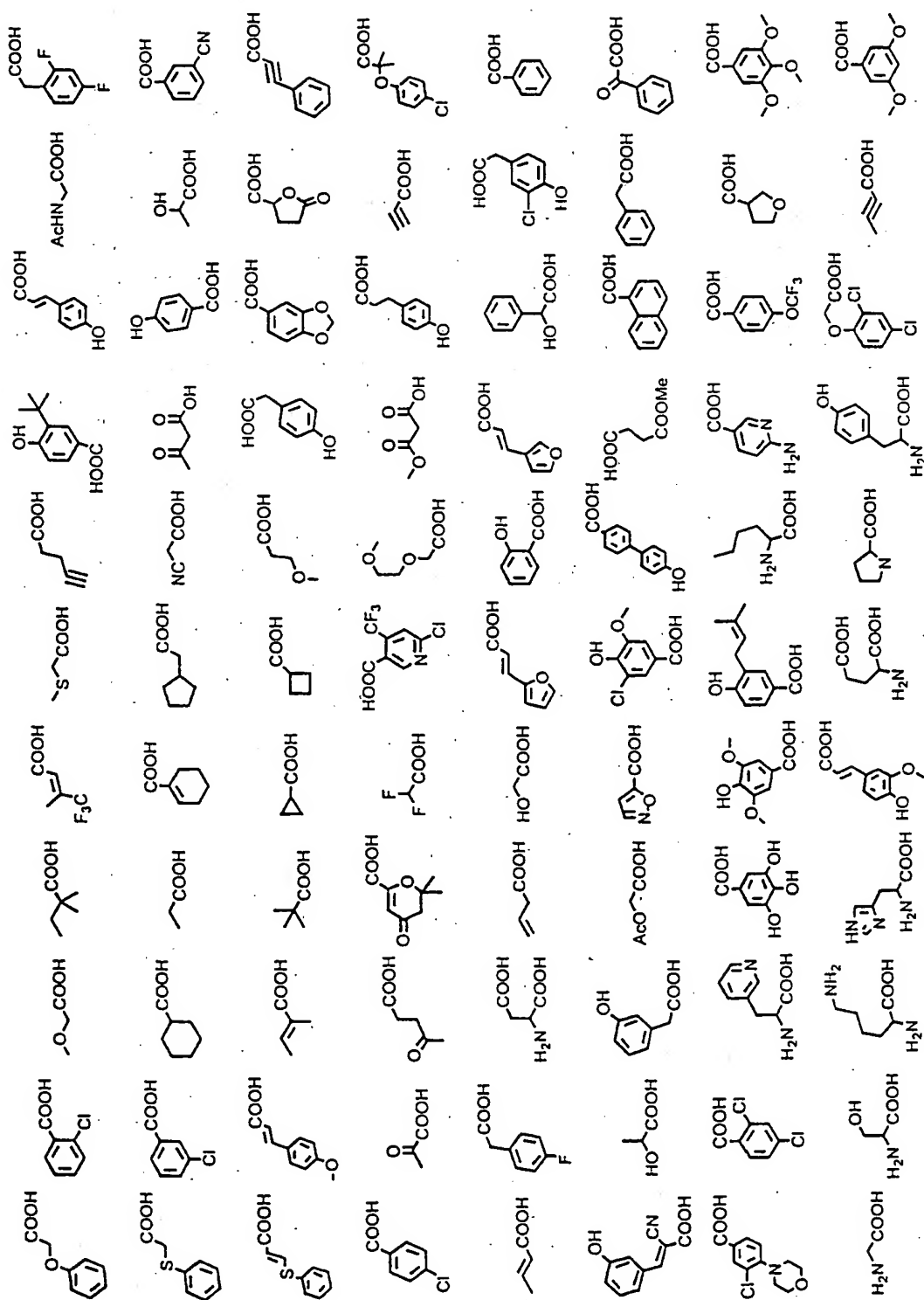


FIGURE 42



**FIGURE 43**



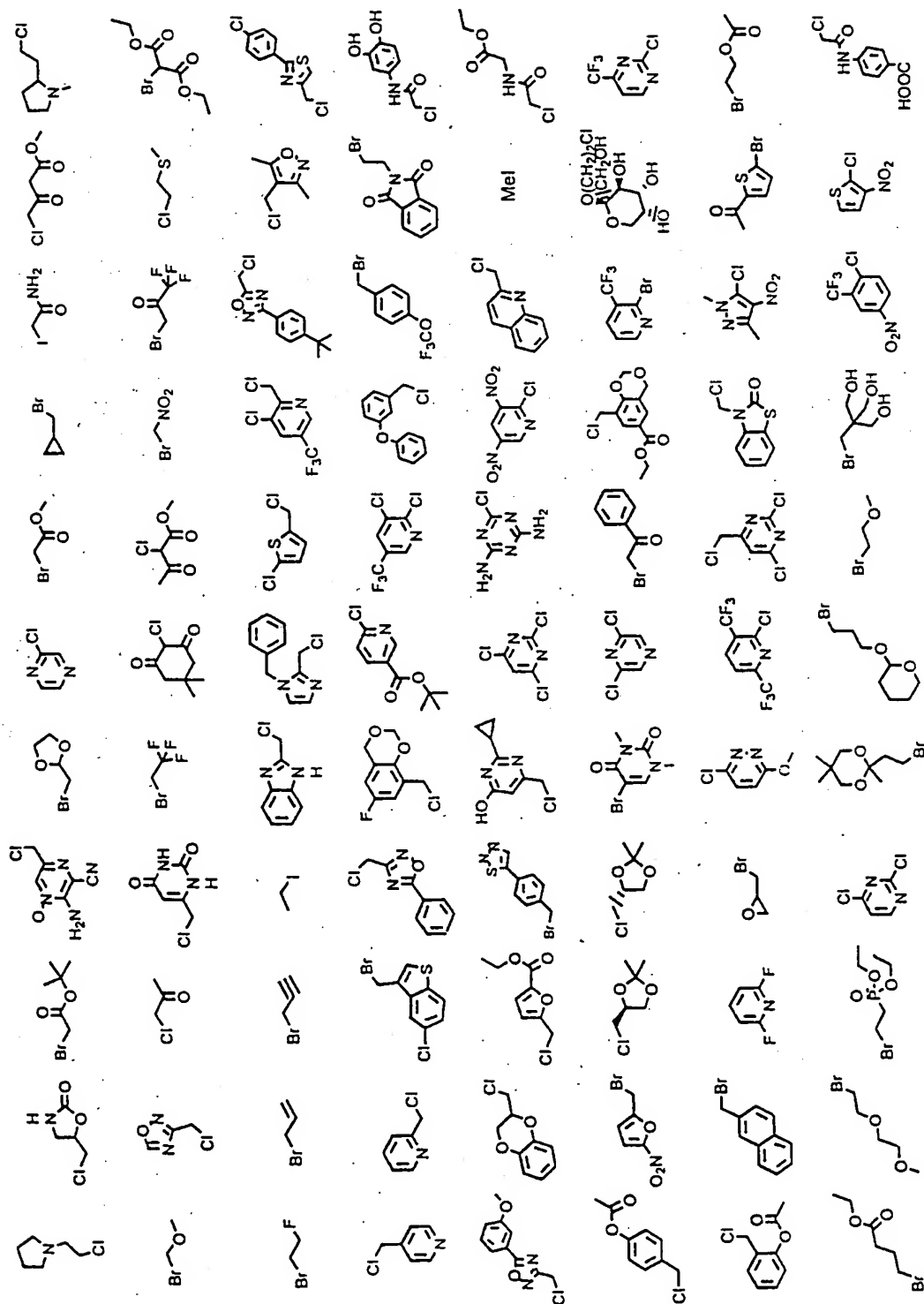


FIGURE 44

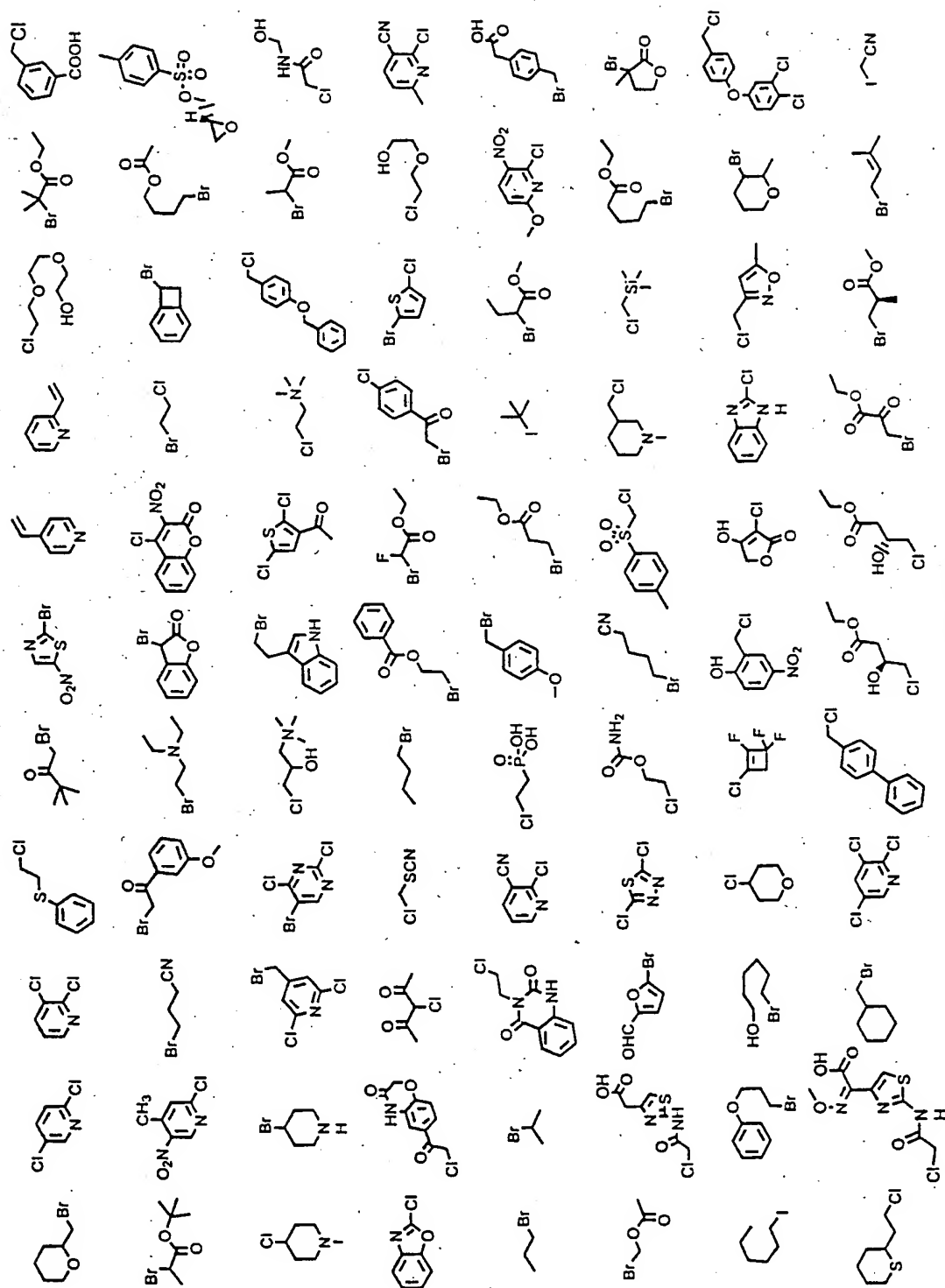


FIGURE 45

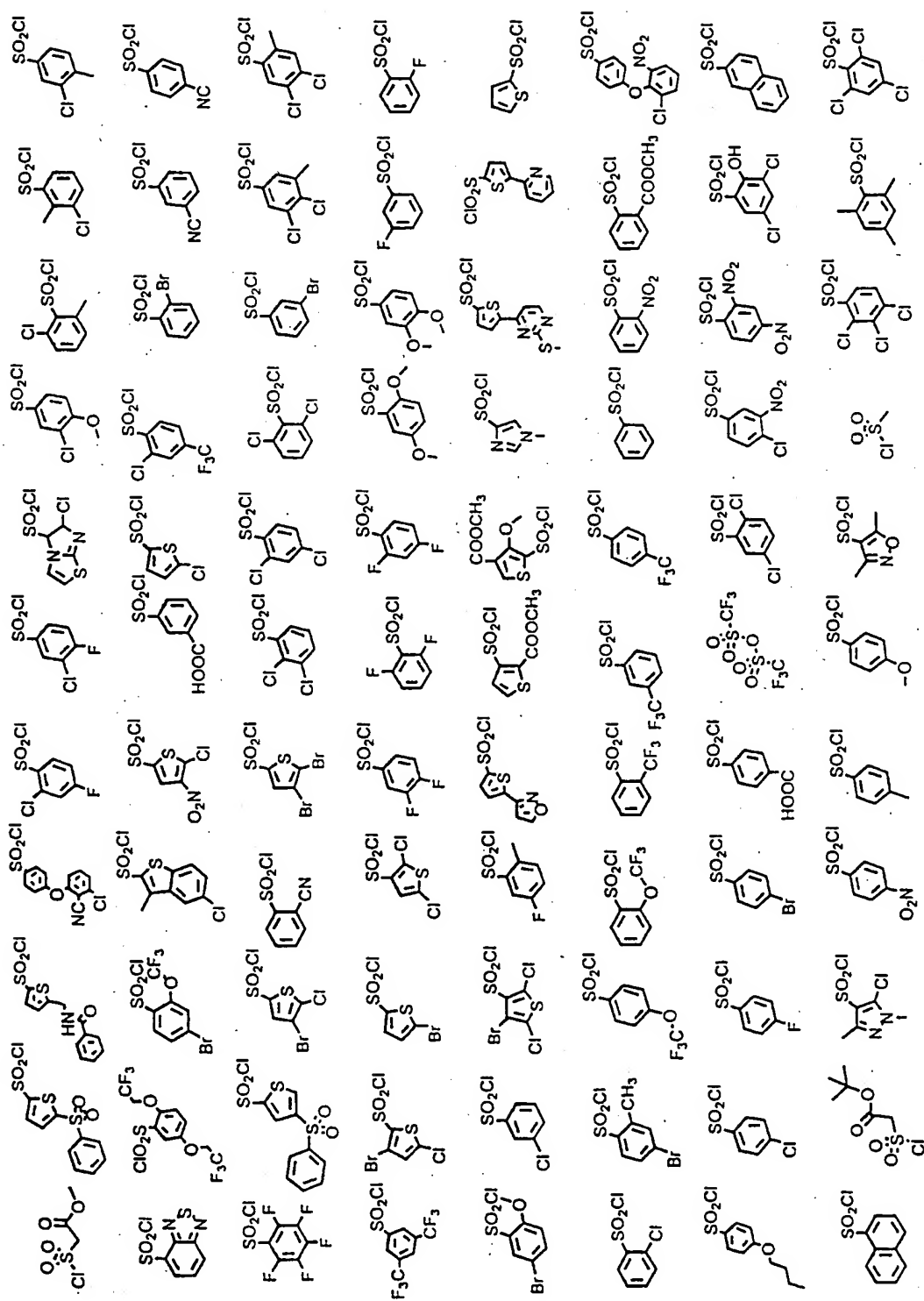


FIGURE 46

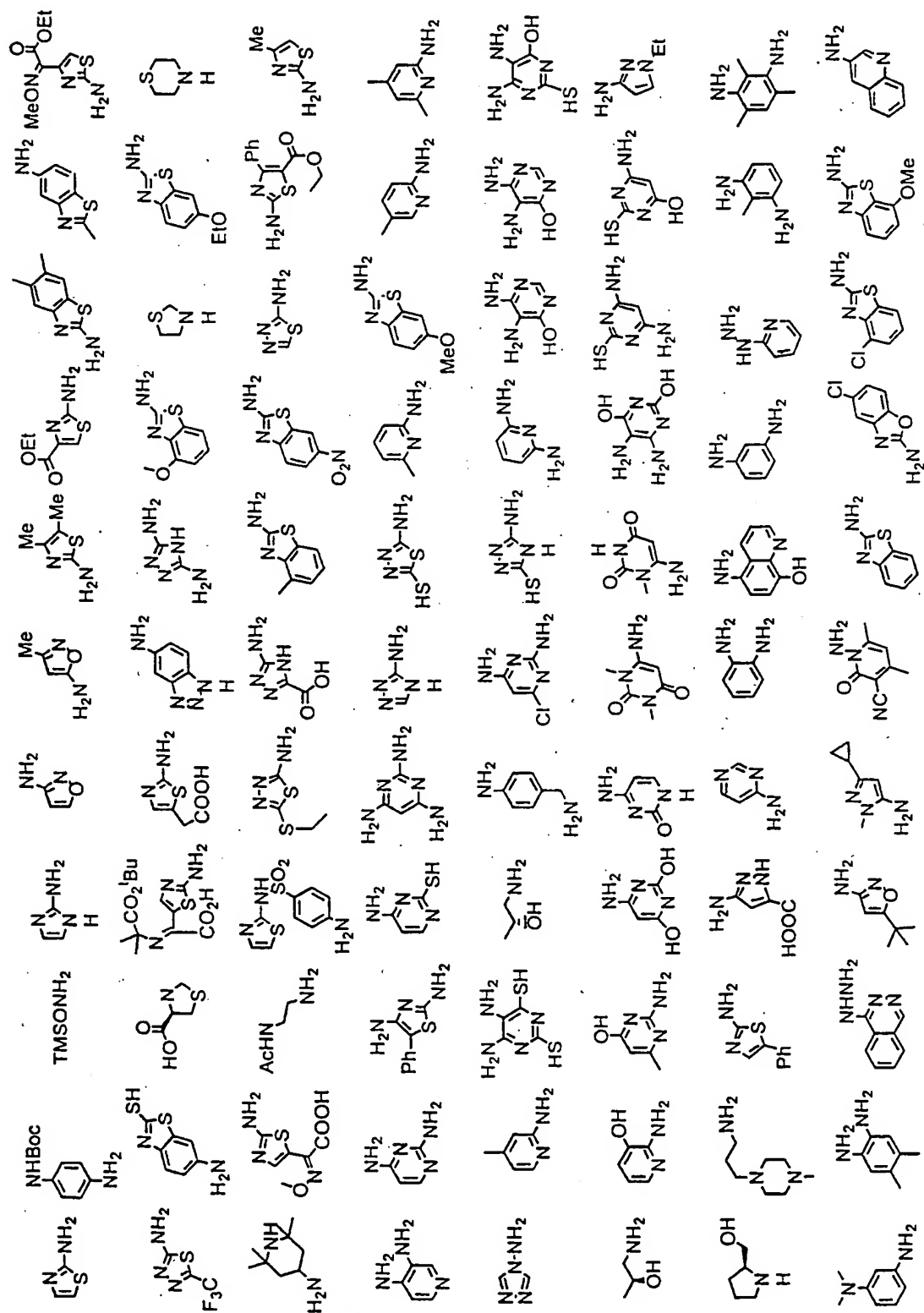


FIGURE 47

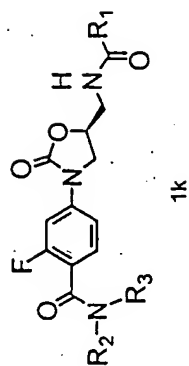
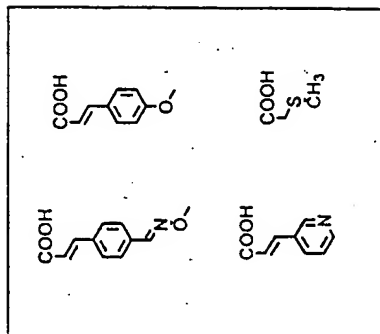
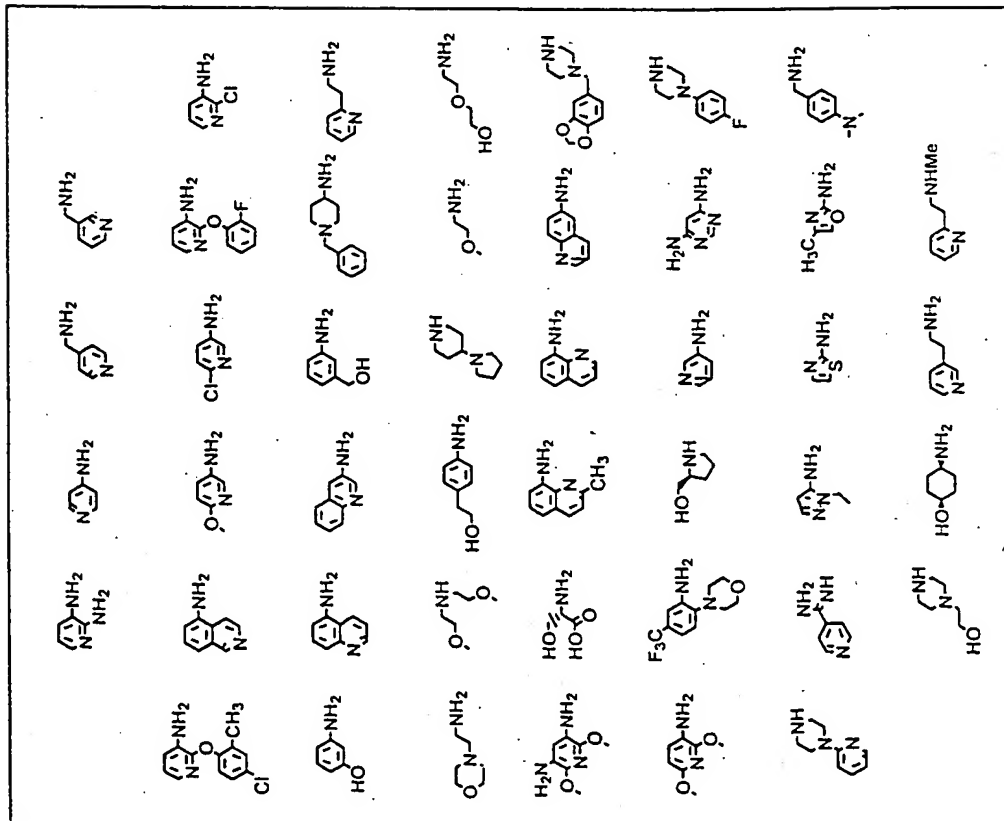
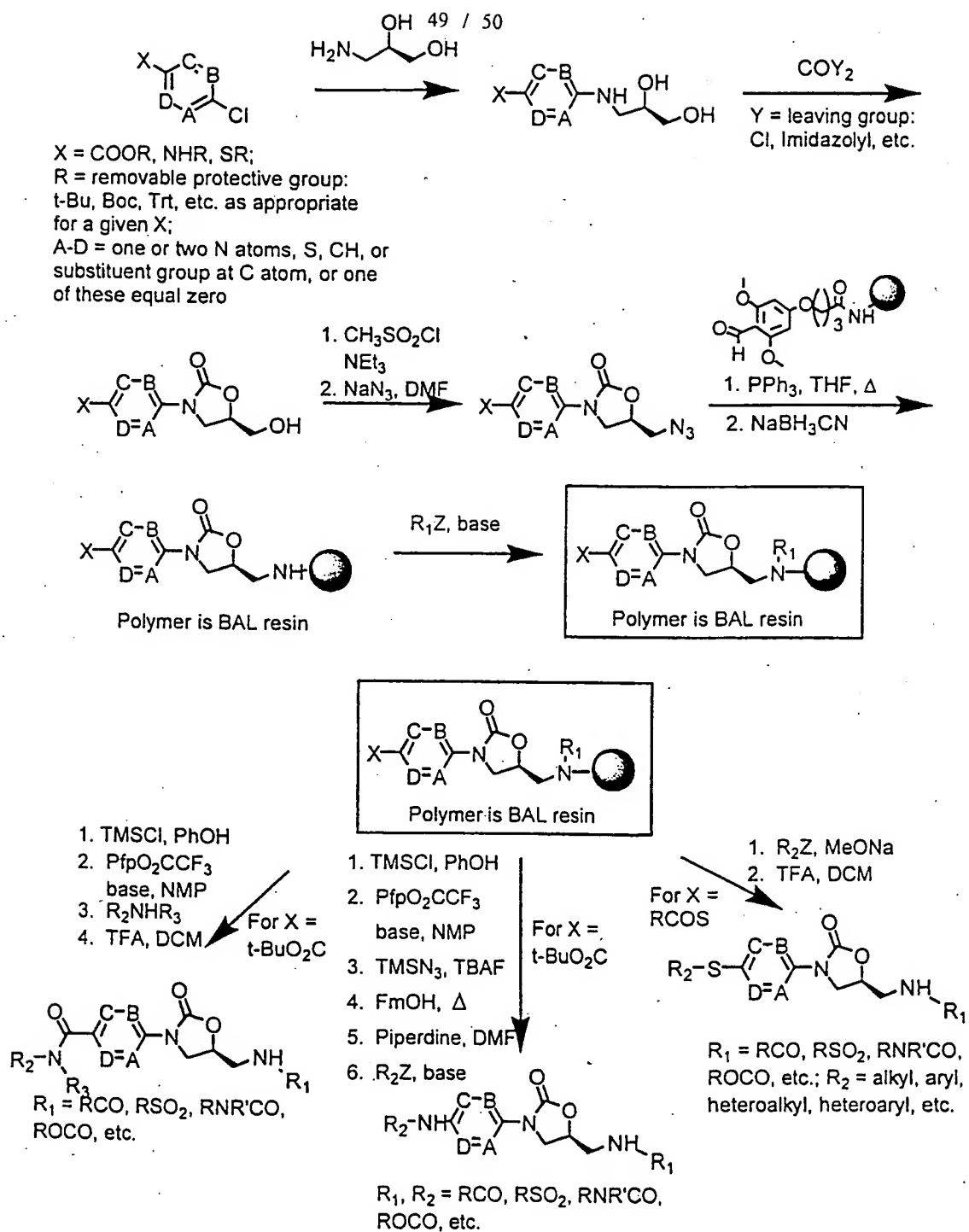
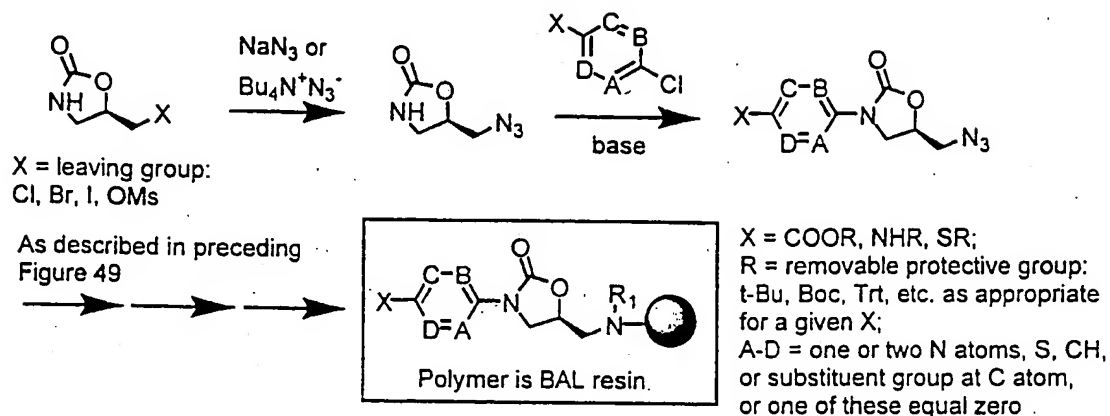
R<sub>1</sub>COOHR<sub>2</sub>R<sub>3</sub>NH

FIGURE 48



## Synthesis from 5-(S)-azidomethyloxazolidinone



## Synthesis from 5-(S)-(protected amino)methyloxazolidinone

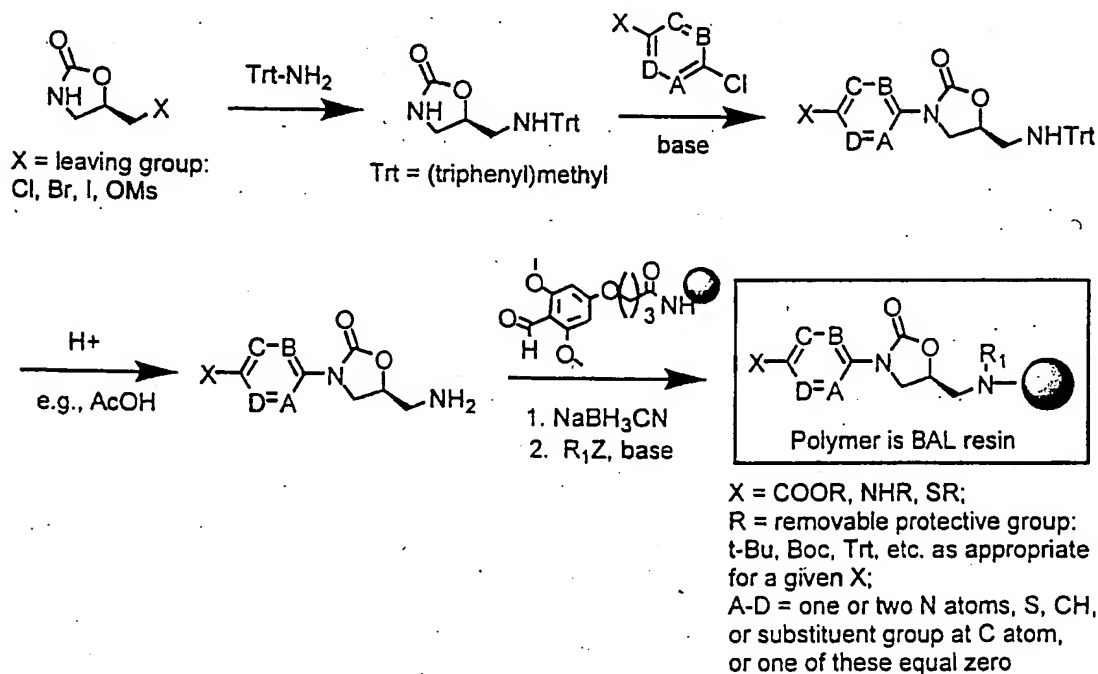


FIGURE 50

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 99/01318

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C07D263/20 C07D413/12 C07D417/12 C07F9/653 C07D417/04  
C07D413/04

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C07D C07B A61K C07F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 30981 A (PHARMACIA & UPJOHN CO) 28 August 1997  see claims	7-9, 13-43, 60-82,95
X	WO 97 21708 A (PHARMACIA & UPJOHN CO ) 19 June 1997  see claims	7-9, 13-43, 60-82,95
X	WO 98 01446 A (ZENECA LTD ) 15 January 1998  see claims	7-9, 13-43, 60-82,95
	-/-	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents :

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Date of the actual completion of the international search

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Henry, J



# INTERNATIONAL SEARCH REPORT

International Application No

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Int. J. Application No

PCT/US 99/01318

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# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 99/01318

## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 95-100  
because they relate to subject matter not required to be searched by this Authority, namely:  
Remark: Although claims 95-100  
are directed to a method of treatment of the human/animal  
body, the search has been carried out and based on the alleged  
effects of the compound/composition.
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such  
an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all  
searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment  
of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report  
covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is  
restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.  
☐ No protest accompanied the payment of additional search fees.

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